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THE AMERICAN

JOURNAL OF PHARMACY

SEPTEMBER, 1920

EDITORIAL.

IS THE PRACTICE OF PHARMACY TO BECOME A NEGLECTED ART?

Under the title "Why Proprietaries Flourish" the following letter is published in *The Journal of the American Medical Association* for June 2, page 558:

"*To the Editor:*—The following experiences seem to add one more to the many reasons offered to explain why proprietaries and ready-made preparations flourish at the expense of the official drugs and preparations: A few days ago I prescribed Troches of Ammonium Chloride, U. S. P., for a patient of exceptional perseverance. The next day he had not yet secured the troches and told me that he had submitted the prescription to seven pharmacies, including the largest and three of the best known and admittedly the best equipped in New York. All told him that these troches were "Not being made any more," and that they were, therefore, unable to supply him. He thereupon communicated with one of the largest wholesale manufacturing pharmaceutical houses in America and received precisely the same answer. I then took the matter up with a first class pharmacist whom I knew and induced him to prepare this difficult(!) troche, for which the U. S. Pharmacopoeia gives the following directions: 'Rub the powders together until they are thoroughly mixed; then form a mass with syrup of tolu and divide . . .'

"Seven pharmacists declined to fill a prescription for an official preparation because they could not buy the preparation from a wholesaler, and it required some persuasion to get the eighth to make the preparation. But even, worse, several of the pharmacists offered my patient some ready-made troche more or less closely resembling the official, or offered compressed tablets of ammonium chloride.

"That this is not an isolated example of what often poses as pharmacy is shown by the fact that I have found it extremely difficult to find a pharmacist who would extemporaneously coat pills with gelatin. Most want the physician to alter his prescription so that one of the ready-made gelatin coated pills can be dispensed, if a gelatin coating is necessary. Some gelatin, hot water, a large cork, and a few domestic sewing needles are all that is required for very satisfactory coating of pills with gelatin, yet few pharmacists seem willing to perform this simple procedure.

"Two other illustrations, not so recent, have come to me from a colleague. A few years ago he was unable to obtain an emulsion of cod liver oil without the hypophosphites because, as both pharmacists said, 'It does not come without hypophosphites.' On another occasion four of the best drug stores in Boston were asked for the Compound Laxative Pill., U. S. P., then official in the Pharmacopoeia. In every case he was told that he must have meant the compound cathartic pill, which in no way resembles the pill he sought.

"With this attitude on the part of the men supposed to be serving the public and the medical profession by the practice of pharmacy, is it any wonder that it is difficult to induce the medical profession to prescribe official preparations or combinations of official drugs in place of ready-made commercial substitutes largely drawn from among the proprietaries or specialties? Real pharmacy by real pharmacists is a necessity if we are to succeed in combating the proprietary evil.

"CARY EGGLESTON, M. D., New York."

By this communication, Dr. Eggleston has performed a service to pharmacy and to a somewhat lesser degree also to medicine. His criticism of the attitude of the pharmacist referred to in his letter, is fully justified by the experiences detailed. Our inclination is to more strongly condemn their failure to discharge their professional obligations as we consider their action as detrimental to pharmacy and deserving censure in a most positive manner and in no uncertain language.

It is evident that Dr. Eggleston is an exception among physicians as his communication demonstrates a knowledge of pharmacopoeial formulas which is certainly unusual among prescribers. After all, can we not trace these experiences to the initial fault, the fundamental error; the defect in the education of physicians by reason of which they become so little acquainted with the official materia medica.

and the formulas and dosage forms for the accepted medicines that many of them almost entirely neglect these for the proprietaries or the ready-made "specialties" of the manufacturing houses which frequently are but other forms for exhibiting the same medicines. If the physicians were properly educated and prescribed the official medicines to the fullest extent possible, doubtless a sufficient number of pharmacists would be equipped to promptly dispense every prescription calling for these.

It is a sad commentary upon the present status of the medical practices that we must admit that a number of the pharmacopoeial preparations, standard remedies, are so completely neglected and ignored by the medical practitioners that some of the druggists appear to have entirely forgotten that the titles and formulas for these are in the U. S. P. These formulas, no matter how desirable they may be from a therapeutic standpoint, are becoming obsolete from non-use and sooner or later must be deleted from the Pharmacopoeia and possibly even from the National Formulary. The existing condition unquestionably calls for corrective measures and these can be effected only by the earnest coöperation of the exponents of the professional practice of medicine and pharmacy.

In pointing out this fundamental error in the medical education of the time, we are fully aware of the fact that Dr. Eggleston in this communication points out, in a courteous yet forceful manner, vital defects in the education and practices of pharmacists. It is not our purpose to excuse these in the least, neither is it our intent to minimize the force of his criticism, but rather add thereto. It is deplorable that in this progressive and scientific age and after nearly a century of systematic efforts in behalf of pharmaceutical education, such episodes can be recorded. It is almost inconceivable that such incidents could occur in the large cities like New York and Boston and be reported as happening in the "largest," "best known" and "best equipped" pharmacies in the leading American metropolis. In an urban community or in a back-wood's district one might be more charitable in his criticism. From the view point that we entertain of the ideals of professional pharmacy, we must attribute the experiences described by Dr. Eggleston either to woeful ignorance, professional stupidity, business inaptitude or unsophisticated indolence and none of these are valid excuses or excusable.

The official troches of ammonium chloride require no special apparatus, unusual materials or exceptional skill for their prepara-

tion and even if a lozenge board or a lozenge cutter is not in the equipment, the troches can be readily made extemporaneously with the common utensils, mortar, pestle and spatula which are necessarily at hand in every drug store. The Pharmacopoeia, presumable for self-evident reasons, gives very simple instructions for the manipulation in this formula and leaves to the judgment and the art of the dispenser the method of dividing and even the shape of the troche so that he is at liberty to improvise in these matters as occasion may require. The preparation of emulsions of cod liver oil, compound laxative pills and of gelatin coated pills on prescription, requires no unusual skill or exhibition of the art of the apothecary and every graduate of a school of pharmacy should have been taught in the school not only the theories of such operations but acquired by practical work the skill essential to compounding such on physician's prescriptions. The processes named are merely practical exhibitions of the art of pharmacy and not beyond the ability of a tyro.

They are in the line of the professional duty of the pharmacist and the service which he owes to society and constitute his part in the great medical professions. When these so called pharmacists failed to perform their bounden duty and to practice the true art of pharmacy, they injured not themselves alone but the entire profession of pharmacy. Without the proper exercise of the art and the development that comes from actual practice there can be no progress of the profession. It is humiliating to those who have devoted their best efforts in behalf of pharmacy that such incidents should occur. The pharmacists of America and especially those associated with pharmaceutical education, should take from Dr. Eggleston's communication a timely lesson as to the insufficiency of, and defects in pharmacuetical education and practices.

G. M. B.

A QUESTIONABLE DECISION.

Under the caption "Copyright Trade Mark Declared the Sole Property of the Centaur Company," the *Canadian Druggist* for July, 1920, informs its readers that: "In the Practice Division of the Superior Court, Mr. Justice Duclos delivered judgment in the case of the Centaur Co. *vs.* the American Druggists' Syndicate, Ltd., enjoining the use of the name Castoria in connection with the sale of any medical laxative preparation not manufactured by the Centaur Co."

Upon the text of this decision as given in the editorial the following comments are made.

"The title of the editorial, and the comments of the editor, and also the decision of the Court are at variance with what seems to be the law relating to copyright, patents, and trade-marks, not only in the United States, but in Great Britain, and its Colonies. The editor seems to have a confused idea in regard to copyright, or the right to copy the published writings of writers and the unpatented discoveries of inventors—rights possessed by everybody—and the exclusive right naturally possessed by every manufacturer to so mark his brand of goods as to inform the public concerning their source of manufacture. The text of the 'judgment' indicates that Mr. Justice Duclos shares in this confusion of mind.

"As stated in the Report of the Commissioners Appointed to Revise the Statutes Relating to Patents, Trade and other Marks, and Trade and Commercial Names, under Act of Congress Approved June 4, 1898 (Senate Document No. 20), p. 91: 'There is no such thing as an exclusive right to any particular branch of industry. Any article of manufacture, unless it be protected by a patent, may be made and sold by any person. The only restriction is that each party shall stand upon his own merits, and none shall be permitted, by the use of marks or symbols, to pretend that the goods offered by him are the products of another.'"

The necessities of spoken and written language, the necessities of science, of the arts and manufactures, and of commerce, require that each new invention shall be provided with a name of its own by which it may be recognized and dealt in, and that such name shall be free to the use of all who have the right to make and deal in the article. This self-evident fact was well expressed by the Court in Leclanche Battery Co. *vs.* Western Elec. Co., 23 Fed. Rep., 227, as follows: "When an article is made that was theretofore unknown, it must be christened with a name by which it can be recognized and dealt in, and the name thus given it becomes public property, and all who deal in the article have a right to designate it by the name by which it is alone recognizable."

Mr. Justice Duclos says: "After a careful consideration of the evidence, authorities and arguments submitted to me I find:

"1. That the petitioners secured a valid and still existing trade-mark in Canada."

Comments.—Castoria is the name of the product sold by the

Centaur Company, just as it would be if they were selling salt or sugar under the names "salt" and "sugar," respectively. It is axiomatic that a name cannot at one and the same time perform the function of a brand mark, and the name of the article itself. During the life of a monopoly, no matter how created, whether by secret formula or patent, only one brand is possible, and, therefore, the name given to the product can only distinguish between the product itself and other products of unlike character. But when the monopoly ceases, either by the disclosure of the trade secret, or by the expiration of patent, it may become advisable to adopt a word or mark to distinguish between the original brand, and other brands of the same article on the market, because the name of the article itself cannot perform that function. The name "salt" cannot distinguish between the various brands of salt on the market, and the same is true in reference to the name "sugar." And now that the working formula for the production of castoria (which was of course published by the inventor in his application for United States patent) is common property, any person has a right to manufacturer castoria and sell it as castoria.

Certain trade mark lawyers have claimed that the commercial introducer of a new product can, by registering the name given such product as a trade mark, secure exclusive ownership of such name. On this hangs the entire fabric of the so-called proprietary medicine system. But this is an absurdity: The logical outcome would be to force each manufacturer of an unpatented product to coin a new name for it until the common language would become so loaded up with synonyms as to make it impossible for anybody to remember them. It would, in fact, necessitate a library building as large as a city public library to accommodate the dictionaries required. This is illustrated by "hexamethylenamine" for which there are already more than fourteen synonyms including "aminoform," "urotropin," "cystamin," "cystogen," etc.

"2. That the respondents have, and are intending to infringe this trade-mark."

Comments.—If the American Druggists' Syndicate is using and intends to use the name "Castoria" in such manner as to deprive the Centaur Company of its rights, or to deceive the public, then this statement of Mr. Justice Duclos is in accord with the facts. On the other hand, if it is using the word "Castoria" as the name of a product which is common property, and which all have an equal

right to make and sell under the name "Castoria," then the American Druggists' Syndicate in going into competition with the Centaur Company is acting within its rights, unless they are deceiving the public by imitating the packages of the Centaur Company. The correctness of the above statement is recognized by *Standard Remedies*, for Dec., 1915 (*Standard Remedies* is published in the interest of the manufacturers and jobbers of proprietary medicines, cosmetics, etc.).

In referring to the dangers attending the Goldwater Ordinance, the editor warns manufacturers to be careful not to jeopardize their trade-mark rights, by complying with the requirements of the New York health board until they are compelled to do so, if they ever are, by the decision of the Courts of last resort.

In support of this warning the editor quotes the following paragraphs from Cyc. 38–740:

"The name of a secret or proprietary preparation is descriptive thereof, and hence is not a valid trade-mark. Anyone who discovers the secret and makes the goods according to the formula may use the name to describe the goods. A contrary view has been expressed, and such names declared to be valid trade-marks, but such cases must be deemed instances of the broader doctrine of unfair competition. Of course the name may not be used to pass off spurious concoctions as and for the genuine preparations."

To again quote from Cyc. 38–835:

"The name of a secret and proprietary preparation will be protected against unauthorized use or imitation as the name of some other different preparation of like kind sold in competition, but not made in accordance with the formula of the original and genuine article, even though the labels and wrappers are entirely different, because such a use is necessarily false and deceptive.

"But such names are generally descriptive and therefore may be used by anyone who discovers and knows the secret of the composition of the article and makes his own article according to the original formula. If such is the truth a subsequent user of the same must add some distinguishing statement showing that the article is his own production of the article known by that name and he must not imitate the dress or the makeup of the goods in addition to using the name, or do any affirmative act calculated to deceive the public and pass off the goods as and for the previously known goods."

"3. That the name 'Castoria' is a purely fancy name in no way descriptive of the article."

Comments.—A fanciful name is one that is used fancifully. Is the name "Castoria" being used fancifully by the Centaur Co., or is it being used descriptively? The word "Castoria" in itself, means nothing, and the same is true of the words "cat," "dog," "hat," "buggy," "piano," and "porcupine." In themselves these words may be with equal proprietary called fancy names. But when they are applied to the various things which have become known by these names they become, by such use, descriptive nouns of the common language. In this way "Castoria" has become just as descriptive of the medicinal preparation known as Castoria as the name "salt" is descriptive of salt, and the name "sugar" is descriptive of sugar.

"4. That in Canada the word 'Castoria' has acquired a secondary meaning identifying the article sold under that name as the manufacture of the petitioners."

Comments.—Now, when it is considered that the function of a trade-mark is to distinguish between brands, and that the name of an article cannot at one and the same time perform the function of an appellative and a brand mark, it becomes at once apparent that the name "Castoria" is not being used by the Centaur Co., as a trade-mark, and, therefore, is not in fact a trade-mark. The only reason why the name "Castoria" exclusively distinguishes the manufacture of the Centaur Co. is because the Centaur Co. has monopolized the sale of the product known as Castoria. Until the monopoly ceases there is nothing to distinguish it from. But when someone else commenced to make Castoria then two brands of Castoria came into being, and it logically follows that both brands must be sold under the generic name, *i. e.*, "Castoria," otherwise, the manufacturer of second brand is deprived of his rights, for he has an equal right to manufacture and sell Castoria, and would be deprived of that right if he could not sell it as "Castoria." It is evident that the manufacturer of the second brand would be forced to educate the public to use another name for "Castoria," claiming the preparation under the new name to be the same as that being sold by the Centaur Co., under the old name, and would also be obliged to do so under the unfair handicap of charges of fraudulent imitation.

"5. That no one in Canada can sell or offer for sale a senna laxative under the name of Castoria, without misleading the public

into the belief that they are selling the petitioners' goods while passing off their own."

Comments.—All that is required is not to imitate the packages of the Centaur Co., but to offer the product as Castoria under the label and package of the American Druggists, Syndicate, just as would be done in offering fluidextract of senna, or syrup of squill by competitors in the manufacture and sale of these products.

"6. That the article which the respondents are putting on the market as 'Castoria,' while very similar, is not the same product as manufactured by the petitioners, and, therefore, cannot be truthfully called 'Castoria.' "

Comments.—As already stated, the working formula for the manufacture of "Castoria" was published by the inventor when he obtained his United States patent, and is obtainable from the Patent Office for a nominal sum. If a person skilled in the art of pharmacy cannot reproduce the identical article by using this formula then the original patent was obtained by fraud. In that case neither the inventor nor his agents can go into court with clean hands to defend a suit for infringement. It might be well for the American Druggists, Syndicate to investigate this phase of the subject.

FURTHER COMMENTS AND SUGGESTIONS.

Contrary to general belief names cannot be copyrighted. To correct this misapprehension the Librarian of Congress issued circular number 19, which reads as follows:

"The Copyright laws contain no provision under which protection can be obtained upon a mere name or title. Entry cannot therefore be made in the Copyright Office for coined names; names of articles of manufacture; names of games or puzzles; names of substances, names of products, or names of medicines."

Neither can a name be patented. Its registration in the Patent Office as a trade-mark does not confer any right to its exclusive use as the name for an article of commerce. Such registration serves to give notice that the name registered is claimed as a trade-mark. If it is afterward used as the name of the article itself it becomes a title and not a trade-mark.

The same trade-mark may be used by as many manufacturers of different brands of goods as there are classes, for example the word "star" or the picture of a star has been registered for not less than four hundred classes of goods. As the classification of goods in the

Patent Office is merely arbitrary it is quite important, therefore, that a manufacturer should, for his own protection, accompany the word mark or brand name with the name of the article, on labels and in advertisements, so distinguished between them as to make it clear which name is claimed as a trade-mark, and which is the name of the article itself.

It was stated in a decision of the board of Examiners-in-chief, and appellate tribunal of the Patent Office, in the case of Caffall, MS. Vol. 18, p. 322, that:

"It was never intended that any new composition of matter or mixture of simples should be the subject of monopoly. If rhubarb and senna, or calomel and jalap were for the first time put together, he who should do it, whether regular practitioner, or quack, would not be an inventor or discoverer under the law. If done by a doctor it would only be the exercise of ordinary professional skill; if by another, it would be but an ignorant jumble of things having supposed virtues and benefits to be obtained by the union of known drugs."

A scheme is on foot to obtain such objectionable monopolies, and their protection by the Courts, by creating a system of patenting names in each country, and then by means of international treaties to form a union for the commercial control of such names throughout the world. Some of the Latin countries have already adopted this scheme. Further information concerning it may be obtained by consulting the Report of the Commissioners Appointed to Revise the Statutes Relating to Patents and Trade-marks (Senate Document No. 20), referred to above. The following paragraphs are copied from a report of a draft presented by M. Ch. Jagerschmidt, a French delegate to the Conference which met at Paris, Nov. 4, 1880, for the purpose of taking preliminary steps leading to the adoption of the International Convention at Paris, 1883, having as its object "the protection of patents for inventions and other industrial property." The Convention was ratified at Paris, June 6, 1884, but was not adhered to by the United States until March 29, 1887, and proclaimed by the President, June 11, 1887. Still our Government sent a delegate to the first conference under it, held at Rome in 1886.

The following paragraphs are copied from Mr. Jagerschmidt's draft:

"Art. 6. Every production bearing unlawfully either the mark of a manufacturer or of a merchant located in one of the countries

of the Union, or an indication of origin in such country, shall be prohibited entry in all the other contracting States, excluded from transit and from storage, and may be subject to seizure followed, if necessary, by a suit in court."

"Art. 8. The ownership of a commercial name shall be guaranteed in all the States of the Union without distinction of nationality and without obligation of deposit, whether or not it forms part of a mark of manufacture or of commerce."

"Articles claimed to be infringements may be seized in the inclosure of the expositions."

"The expense to which this institution shall give rise shall be borne by all the Governments of the contracting States."

The attempts to create a system of perpetual monopoly of inventions and alleged inventions by commercial control of their currently used names, and the establishing of an international method for obtaining proprietary rights never intended by the patent and trade-mark laws either in this country or in any other civilized country are still going on.

CONCLUSIONS.

Proper discrimination is not exercised by the Patent Office in regard to patenting inventions and registering trade-marks. Patents are allowed which should never have been granted. Names are registered as trade-marks with the intention of using them afterward as titles for the purposes of monopoly. During the Great World War it developed that more than 17 millions of dollars worth of patents for synthetic chemicals had been obtained by fraud. Inquiry reveals inadequate facilities and dearth of skilled help at the Patent Office through insufficient appropriations.

Are we to sit by indifferently and permit a group of patent lawyers, "proprietary" manufacturers and advertising firms to establish an international union for the commercial control of the drug business throughout the world?

F. E. STEWART, PH.M., M.D.

VISIT TO A BELLADONNA PLANTATION.

It was the privilege of the editor and several friends to visit the Belladonna fields of Messrs. Johnson and Johnson at New Brunswick, N. J., and to observe on a July day many acres of these plants under experienced cultivation. At this time, they were at their best and

in full bloom and the cutting of the tops was in process. In certain fields, plants of two and three years' growth were seen and in others those of the first year. All of these presented a healthy aspect, bespeaking care and the application of scientific methods to prevent the ravages of insects and to obtain the best results in yield and product.

We were equally fortunate in being able to observe the methods used for the extraction of the green herb and of the roots in the laboratory. The Lloyd method of alkaloidal extraction and the Lloyd apparatus for the use and recovery of the volatile solvents being used with satisfactory results.

We appreciate highly the courtesy shown and also the opportunity of inspecting the factory and seeing at first hand the scientific methods adopted by these manufacturers throughout their plant from the purification of the water supply used to the testing, chemically and bacteriologically, of the finished products.

G. M. B.

BELLADONNA CULTIVATION IN A PRACTICAL WAY.

By Fred B. Kilmer, Ph.M., and Ralph O. Smith, Ph.D.

The cultivation of medicinal plants has been urged in the pages of the Journal for a generation. It required a world catastrophe, however, to really quicken interest and place it upon a stable basis. In the earlier period of the war hundreds of growers, either in a large or a small way, embarked in the enterprise without experience and without adequate patience to obtain results. Under these conditions results in many instances were disappointing.

A notable feature of the work has been that the growers who have succeeded were those who approached the problem from an entirely different angle. They were obliged to eliminate the factor of cost, and to solve their problems in a spirit of service, rather than in a spirit of gain. It was necessary to produce drugs, whatever the cost, and they have been produced. It has been worth the effort, and the world has been enriched by the outlay.

The World War caused a scarcity of belladonna, as well as of other drugs, and the culture of this plant has become quite extensive throughout the United States.

The records which follow embrace a summary of belladonna cultivation at New Brunswick, New Jersey, which was begun in

1900, and has continued since that time. In 1919 there were upwards of sixty acres, and there is about the same amount in the field the present season (1920). From these fields we have been pleased to supply seeds for experimental cultivations in various parts of the country, and to give growers the benefit of our experience.

Method of drying belladonna herb by hanging in warehouse.

Climate and Soil.—Belladonna can be grown in every State in the Union, and in Canada. It is naturally a shade plant, but it grows well in open localities having cool nights and considerable atmospheric moisture, such as abundant fogs. When well rooted, artificial soil moisture (irrigation) is not essential. When soil moisture is too abundant it is harmful. The plant does not do well in localities where there are long periods of intense sunshine.

Seedlings require abundant soil moisture until they are well rooted. Continued dry weather and sunshine are harmful. When heavy rain is followed by hot sunshine there is apt to be a scalding of the plants, and it is for this reason the ground should be well drained.

In our plantings we have found the plants made slow growth during the hot days of July and August, and that their most abundant growth was during the cool, moist nights in the latter part of August, and in the months of September and October.

The following table gives the mean temperature and rainfall

for this locality during the growing months for the last four years. This climate is not an ideal one for the growing of this plant.

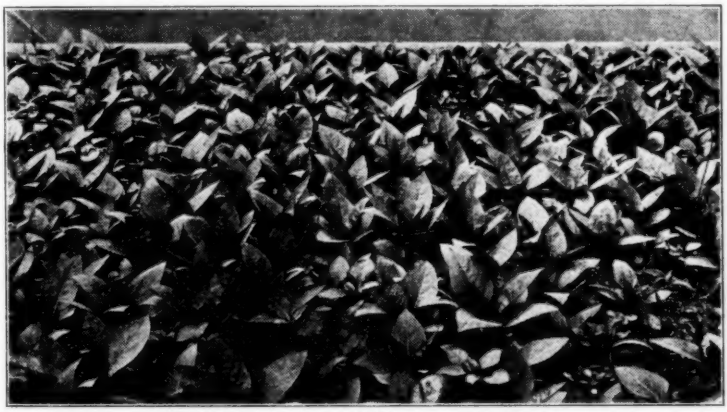
	Precipitation. Inches.				Mean Temperature.			
	1916.	1917.	1918.	1919.	1916.	1917.	1918.	1919.
Apr....	3.52	2.49	3.11	2.73	48.4	48.4	50.0	50.0
May...	3.17	3.87	5.11	5.11	61.6	53.9	65.8	60.7
June...	3.39	3.62	....	5.31	64.7	69.0	67.0	70.2
July...	6.96	6.97	4.54	8.33	74.2	74.0	73.2	73.6
Aug....	2.61	0.87	2.55	6.30	73.6	74.2	75.0	70.3
Sept....	2.53	3.63	3.32	2.01	65.6	61.4	62.7	66.0
Oct.....	1.38	7.34	1.30	3.13	55.5	51.4	57.4	60.4

In localities where the frost penetrates deeply into the ground, roots must be taken up in the Fall and protected against freezing, and in turn re-planted in the open ground in the Spring. This is the method which we follow.

Portion of field of first-year belladonna plants. Inset shows an enlarged branch in fruit and flower.

The plant seems to thrive best in deep, well drained, moist loam, with an abundance of lime. After many attempts at soil fertilization, it was found that stable manure was the best fertilizer. Various forms of fertilizer mixtures, such as are used in drug gardens, will increase the growth of the plant, but apparently will have but little effect upon the alkaloidal content.

Cultivation.—So far as we are aware, no successful cultivations have been made on this Continent by sowing the seed in the open ground. Seeds of belladonna germinate very slowly. After various attempts to hasten germination by the application of chemical and mechanical measures, we found the most satisfactory method was to sow the seed in the cold-frame in December, and allow them to lie dormant until February. About this time they begin to come through and, if the weather is warm, by April they are ready to transfer to flats. The use of a greenhouse facilitates germination, and the plants are more advanced for transference to the field.



Belladonna seedlings in greenhouse ready for transplanting.

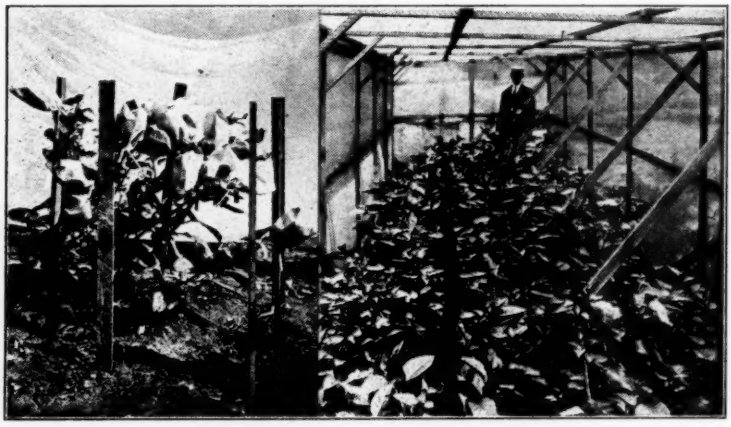
Whether the cold-frame or hothouse method is used, it has been found necessary to transfer the seedlings to flats or pots. While the potting method might be preferable, as giving a more firm root, it entails a greater amount of labor and enhances the cost. (Our potted plants have cost from ten to fifteen cents each.) The seedlings are set out three feet apart, in rows also three feet apart.

Where roots are carried over from one season to another, the problem of placing them in the field is more simple. Here it is only necessary to dig a hole in the ground, and to cover the root to a depth of one or two inches.

In using the roots which have been carried over, the crowns can be divided into from two to five pieces, and each part will give a thrifty plant, especially if large crowns are used. Crowns and

roots are planted more or less like potatoes. The plants are put three feet apart with four feet between the rows.

Cultivation is necessary to keep down the weeds, and to keep the soil fine and well stirred. Irrigation has a tendency to increase root development. If used at all it is only necessary for first-year plants; second- and third-year plants penetrate sufficiently to secure ample moisture. Irrigation increases the tonnage, but not the alkaloidal yield.



Growing belladonna under canvas shade.

Harvesting.—From the first-year plants at least two crops of leaves can be gathered; from second- and third-year plants, two to four cuttings are usual. Harvesting is generally done at the time when the plant is in full flower. At this time the leaves are apt to be the highest in alkaloidal content. To retain the bright green color, which seems to be desirable in the market crop, the leaves should be kept in the shade and dried quickly by the aid of heat. In using artificial heat it is usual to begin with a moderate heat, and gradually increase, some operators reaching as high as 160° F. Other operators have made a great success by beginning a dry process with a high heat —160° F. to 180° F., this for a few minutes only, then the leaves are passed through a moderate heat. This completes the process.

In California they are able to dry the leaves in the sun. In our locality we meet with rain and lack of sunshine sufficient to prove disastrous.

When the leaves and stems are to be used they can be dried in a manner similar to tobacco, but under this condition the leaves will turn brown. The demand for the bright green color in the leaves of belladonna, and other plants, seems to have no valid reason, except custom. The presence of a high content of chlorophyl in pharmaceutical preparations is at times embarrassing.

Trench in which roots are buried for protection against frost.

A very acceptable supply of herb can be secured by a process of "curing," which eliminates the green color, and gives a fairly uniform product of a brown shade.

In gathering roots they are usually plowed from the ground late in the Fall. The larger roots are split, and they are then washed and dried.

In all parts of the country belladonna has been reported to have been attacked by many forms of disease, and by insects. In the early years of our work potato bugs and other species of insects were very troublesome; later the plants seemed to acquire a resistance to insect enemies.

During very hot days the lower leaves of the plant, near the ground, are often killed by the sun's rays. Spring frosts will kill off the leaves and young shoots and, if severe, may be disastrous to the entire plant.

Yield.—The yield of leaves and stems is greatest in the second- and third-year plants. The roots and stems of old plants are apt

to become woody and fibrous, with a decrease in the quantity of alkaloid.

Stockberger reports the results obtained from sixty growers of belladonna for 1917, as approximately 600 pounds of belladonna herb, and 164 pounds of root per acre. Reports have been made of first-year plants where two cuttings of the plant yielded 1300 pounds of herb, dry weight, and where second-year cuttings of the herb yielded over one ton, dry weight.

In our work we have estimated our results upon the yield for the season per thousand plants, rather than by acreage. Our estimates are made on the weight of the plants in their green, or undried, state.

HERB YIELD PER THOUSAND PLANTS (GREEN).

	Lbs.
Second-year plants.	
Herb	1177
Alkaloid	0.891
First-year seedlings (potted plants):	
Herb	527
Alkaloid	0.313
First-year seedlings (cold-frame plants):	
Herb	534
Alkaloid	0.289

From this showing the greatly increased yield of plants in the second year is manifest. It is also shown that the potted plants from the greenhouse give but a slightly larger yield. The loss of moisture during air drying, based upon the entire crop of herb, averaged 84.07 per cent.

ASH IN AIR DRY DRUG.

	Highest Per Cent.	Lowest Per Cent.
Herb.		
Three year old plants	13.15	8.62
Two year old plants	17.53	11.68
First-year seedlings (potted)	14.47	10.10
First-year seedlings (cold-frame)	17.54	12.77
Roots.		
Three year old plants	8.97	
Two year old plants	15.09	
First-year seedlings (potted)	7.88	
First-year seedlings (cold-frame)	8.81	
Whole Ripe Berries.		
From three-year old plants	4.04	

The limit of the U. S. P. for belladonna leaves is "not more than 20 per cent. of ash"—for belladonna root "not more than 7 per cent. of ash."

The standard suggested by the American Drug Manufacturers' Association for belladonna herb is "not more than 18 per cent. of ash."

These standards may need to be changed to meet the condition of cultivated belladonna, especially so when cultivated upon soils containing a considerable content of lime and potash.

Belladonna seedling, pot grown.

Cultural Experiments.—Concurrently with other growers, we have attempted to increase the alkaloidal content of belladonna. The experiments have shown that the use of lime is a possible factor. It is well known that in England chalk soil is particularly adapted to the growth of this plant.

Attempts have been made to take advantage of the great variation in the alkaloidal content in individual plants, with a view of developing plants high in alkaloid, either from the seed or crown of those plants which ran high in alkaloidal content. Work of this character is surrounded with great difficulties. It has been found that a slight variation in the condition of growth would cause a marked change in the characteristics of the plant. Only in rare instances would the seeds or crowns carry forward the characteristics of the parent plant. Cross-fertilization between plants high

in alkaloid has brought no tangible results. For the most part plants will breed true only for two or, at least, three generations. So far as our knowledge goes, no hardy strain of belladonna has been developed. Experiments of growing under shade, such as tobacco cloth, while giving a somewhat increased yield, were not sufficiently striking to warrant a continuous use. A number of growers have produced a strain which gives a large leaf.

The Department of Agriculture at Washington has, in a small way, produced a strain of belladonna which will give a larger yield of alkaloid in the leaf and stem, and they are hopeful that this character may be transmitted.

Belladonna Herb.—Growers of belladonna are severely handicapped under present conditions, whereby the leaves and the roots only are marketable.

The Ninth Revision of the Pharmacopoeia required that belladonna folia should be "without the admixture of more than ten per cent. of stems or other foreign matter." Under this standard the grower is deprived of the sale of from thirty to fifty per cent. of the tops.

The relative weights of green herb and root from typical plants is shown by the following figures, which were secured from two or three plants of each lot designated, selected at random at the close of the season. These plants had, of course, yielded from two to four cuttings earlier in the season:

COMPARATIVE YIELD IN HERB AND ROOT (GREEN)

Three year old plants:		Per Cent. Alkaloid.	Grams Alkaloid.
Herb	1744 grams	0.083	1.45
Roots	1188 grams	0.163	1.94
First-year seedlings (potted plants):			
Herb	1144 grams	0.061	0.70
Roots	548 grams	0.159	0.87
First-year seedlings (cold-frame plants):			
Herb	1079 grams	0.062	0.67
Roots	466 grams	0.167	0.78

Numerous authorities have shown that the stems of belladonna equal, and at times exceed, in alkaloidal content the standard of the Pharmacopoeia. Our work has repeatedly shown that the whole of the stems of the plant can be mixed with the leaves—in other words, the entire tops of cultivated belladonna—and fully meet the alkaloidal requirements of the Pharmacopoeia.

Strong efforts are being made to stimulate the cultivation of drugs in this country. To accomplish this every inducement must be made in behalf of the grower. With belladonna, and many other drugs, it may be necessary to revise our standard, the more especially so when such revision does not in any way detract from the medicinal value of the drug.

In respect to belladonna, the American Drug Manufacturers' Association has suggested that belladonna herb, by which term they intend to include the dried leaves and stems, should be made official in the Pharmacopoeia, and allowed to be used for galenical preparations in the manufacture of medicinal products. They suggest that belladonna herb should be inserted in the Pharmacopoeia in addition to belladonna leaves and belladonna root.

Our records for the year 1919 show that the tops of belladonna, including the stems, would fully meet the requirements of the Pharmacopoeia.

The following figures are taken from the records of herb cut from three to six inches from the ground, without any attempt at selection, at such times as we found convenient for gathering, and without any particular reference to the alkaloidal content. This latter for the reason that the drug was to be made into assayed products.

BELLADONNA HERB (AIR DRY STEMS AND LEAVES)—1919.

	Per cent. alkaloid.	
Plot Number.	Highest.	Lowest.
1—500 three year old plants.....	0.491	0.385
2 and 5—50,000 first-year seedlings (potted plants).....	0.473	0.328
7—33,000 two year old plants.....	0.570	0.392
8—1,600 three year old plants.....	0.524	0.520
10—72,000 first-year seedlings (cold-frame).....	0.515	0.305

From the foregoing it will be seen that the entire crop from this 150,000 plants, taken separately or mixed together, would at all times have exceeded the requirements of the Pharmacopoeia, and there would therefore seem to be no good reason why belladonna herb, especially that obtained from cultivated plants, should not be admitted to the Pharmacopoeia under proper restrictions as to alkaloidal content, etc.

Conclusion.—Much progress has been made in the growing and collection of belladonna in the United States. We are no

longer dependent upon foreign sources for such drugs as can be grown in our climate.

We have not yet reached the point where production can be made on the pre-war basis as to cost. In some of the earlier work here outlined, belladonna herb and root cost ten dollars per pound, and owing to labor and other conditions the cost is still high.

There are numerous advantages in the home source of supply for drugs. These include the securing of a higher and more uniform quality from the cultivated plant, and the fact that the drug can be grown, gathered and utilized under scientific control.

Many problems yet remain unsolved, and to these the pharmaceutical worker may well give his attention.

The cultivation of drugs should continue to receive the fostering care of the government, the manufacturer, the dealer, and the dispenser of medicinal preparations.

Wherever possible the standards should be revised, so that we may reap the full benefits to be derived from the American grown supply.

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METHYL ALCOHOL AND ETHYL ALCOHOL: THEIR SOURCES, MANUFACTURE AND USES.*

BY H. R. FRENCH.

METHYL ALCOHOL.

As Wood, or Methyl Alcohol is in such strenuous demand to-day for many manufacturing purposes, owing to the fact that it is the only satisfactory natural source of the methyl, or CH_3 radical, for the manufacture of Methyl Aniline Dyes, which dyes are the principal blue colors, the manufacture of Methyl Salicylate or artificial Oil of Wintergreen, and the manufacture of moving picture film, in which it is used as a solvent, I will treat this subject first.

The destructive distillation of wood is one of the most important of industries. Its economic importance is also great, as wood distillation provides for the utilization of wood waste, and what in

* Read before the meeting of the New Jersey Pharmaceutical Association, Newark, N. J., June, 1920.

years gone by was allowed to decay upon the ground may now be converted into substances necessary and useful to all mankind. No one knows exactly when wood first began to be carbonized and it probably dates back to the beginning of civilization.

At first, however, and even up until approximately a century ago, charcoal was the only by-product obtainable, and it was not known that the vapor, which passed out into the air as "smoke," contained valuable elements which would some day play an important part in the affairs of the world. From the primitive method of burning charcoal in pits to the modern tubular condenser has been a long stride. The tubular condenser is equipped with vertical copper tubes set in specially made tube sheets and surrounded by water contained in a steel tank. The vapor dome and liquor receiver are of copper and a copper trap is provided at the outlet, so that the non-condensable gas may be piped off to be used as fuel. This condenser represents the results of years of research and experience and its high efficiency is a distinguishing feature.

Equipment and Method of Distillation.—Modern hardwood distillation plants are equipped with oven retorts which insure economy, efficiency and surety of operation so essential to the success of the business. In the employment of ovens, the wood to be carbonized is loaded on cars and no further hand labor is required in connection with it, as the cars convey it into the ovens, where it is carbonized, and the resultant charcoal, still on the same cars, is carried through a succession of coolers and sheds, finally arriving at the point where it is transferred to bins or to railroad cars for shipment. Even in this last transfer, hand labor has been reduced to a minimum by the use of some of the modern charcoal unloaders.

Cars.—The first step in the process of distillation is to load the wood on cars. These are made especially for the purpose and are all of steel construction, except the wheels and drawheads, which are of cast iron. The bottom, sides and ends are made of steel bars, securely riveted in place. The sides are quickly detachable to provide for easily loading the wood and unloading the charcoal. The frame is rigidly made of structural steel members, thoroughly braced and securely riveted together. The wheels revolve on specially made bearings, so that the cars are comparatively easy to move. After being loaded with wood the cars are placed in front of the ovens. An oven of 10 cords capacity holds four cars to a charge, and these are placed in a line, all together, on the track lead-

ing to the oven. All the ovens in the plant have the cars so placed before them, usually some little time before the cars are actually run in, so that the ovens may all be recharged, one after another, without the loss of time between. After the cars have been placed in the ovens, the doors on the ovens are closed and the process of carbonization is begun.

Ovens.—Ovens are of varying sizes, from 1 to 10 cords capacity, and usually have a door at each end, so that cars may be run straight through, thus obviating the necessity of turn-tables or transfer tables. Their construction is very strong and rigid. Steel hangers are riveted to the sides, and each hanger is supplied with shackle, U-bolt and suspension washer, the purpose of the hangers being to allow the oven to expand and contract without restriction. Inside of the oven, there is a track for the cars to run upon, and this is made so that it can expand and contract independently of the expansion and contraction of the oven itself. The doors and frames are of cast iron, while the remaining portion of the oven is of steel.

The doors are hinged and when closed are held in place with tapered keys, which are easily inserted and easily withdrawn. The door joints are tongued and grooved and made tight with asbestos packing. They are set in pairs and are bricked in. There is a smokehood to provide egress from the building of smoke and gases which issue from the oven when the discharge end door is open, and the cars are being pulled out. One smoke stack is required for two ovens, and this is placed in the center of the setting. Ducts are provided in the brick work to properly convey the smoke into this stack. Dampers are furnished to give desired control, and individual control of each oven may be had. There are clean-out doors on the sides of the settings, both below and above the ovens. Above the ovens is a drying floor.

Carbonizing Process.—It requires from 18 to 24 hours to carbonize one charge of wood in an oven retort. During this period, the fires in the furnaces are kept burning continuously, but the temperature is allowed to gradually rise from the beginning of a charge to its maximum point, which is reached from six to eight hours after the beginning. Then the maximum temperature is maintained for a variable period, and finally the furnace fires are allowed to go down and the temperature in the ovens gradually decreases until the end of the run. The latter end of the distillation is accomplished by the latent heat in the ovens and their settings.

In from one to two hours after the wood is placed in the ovens, water distillation takes place, and this distillate has an acid content of about 2 per cent. The next to issue from the wood is called "green gas," and this comes freely for about five to six hours. At about 300° Fahrenheit the endothermic reaction begins, but it is more decided at the maximum temperature, which is about 680° Fahrenheit, and at this latter point great care must be exercised that the liquor is not "burned;" that is, the temperature must not be permitted to rise higher, otherwise there will be an undue formation of condensation products. After the wood has been in the heating process for about six hours, the temperature attains an average of about 450° Fahrenheit. About the sixth hour pyroligneous acid begins to flow from the condensers and continues up to about the eighteenth hour. The color of this acid determines whether too much heat is being maintained and whether the wood fibers have been broken down sufficiently. At the latter end of the heating process the distillate forms a considerable portion of tar.

Charcoal Coolers.—The cars, now containing the charcoal, are drawn out of the ovens and into the first coolers, where they remain for a period of about 24 hours, or the length of time required to carbonize the wood in the ovens. The cars are then moved into the second coolers, whore they remain an equal length of time. These coolers are similar in shape to the ovens, are made of steel and are equipped with two doors, one at each end, so that the cars may be run straight through. The coolers are placed in line with each other and with the ovens, and are at the discharge end of the ovens. Coolers are not so heavy in construction as ovens, because their purpose is to radiate the heat from the charcoal and dispose of it in the air. A small vent is provided in each cooler for the vapors to pass out, yet this vent is not large enough to allow much oxygen to enter. The function of the coolers is to prepare the charcoal so that it may be exposed to the air. If the hot charcoal should be taken out of the ovens and left standing in the air, it would immediately ignite from spontaneous combustion. Therefore, it is drawn into the coolers, where it can stand without being exposed to the air, and gradually its heat passes off through the steel of the cooler.

Charcoal Sheds.—After leaving the second coolers, the cars of charcoal must stand in the open air under shed roofs for a period of 48 hours. This is a requirement of the government to insure that there is no danger of spontaneous combustion. After that

time, it may be loaded in freight cars for shipment, but it must be left standing in these cars for at least twelve hours before shipping. Before such precautions were taken, many fires took place and many railroad cars were destroyed.

"Raw" Liquor.—The vapor which issues from the vapor outlet nozzles of the ovens and which passes off from the wood during the process of carbonization enters tubular condensers and is converted into a liquid called pyroligenous acid, or "raw liquor." This does not come from the condensers during the entire period of carbonization, but only from about the sixth to eighth hour on to the end of the run. It is a yellowish green, ill-smelling liquor during most of the run, and towards the latter part its color changes and becomes quite dark. This acid is collected from the condensers by means of a copper branch into a main copper pipe line which passes through the middle of the retort setting and terminates in a wooden sump set in the ground. These sumps are simply for the purpose of providing a reservoir into which the raw liquor may be run.

Gas.—The oven vapor is not all condensable, but one of the products of distillation is wood gas, termed by the manufacturers "non-condensable" gas. This is trapped off at the outlets of the condensers and used for fuel. It has been found that about 11,000 to 14,000 cubic feet of this non-condensable gas are obtained from each cord of wood distilled, and has a considerable value. It is carried from the condensers in copper pipes into a main gas line, and there are also copper distributing lines to convey it to the oven furnaces and to the boilers.

The raw liquor is pumped from the sumps to a series of wooden settling tanks. The pump used for this purpose must be entirely of brass, or brass lined. The brass construction is necessary where the liquor comes in contact with the metal, as the liquor is acid and therefore the metal must be acid-resisting.

Wooden Settling Tanks.—The purpose of these tanks is to allow the tar in suspension in the raw liquor to precipitate. The tanks are so connected together that the liquor passes from one to the other serially, and the pipe connections between them are at varying heights, the connection to the first tank being high up, and the other connections being made gradually lower down, until the connection in the last settler is only about one-third of the distance above the bottom. The first settler accumulates the most tar

and each of the others less than the preceding one, which is the reason for the varying heights of the connections.

Tar Still.—The tar in the bottom of the wooden settlers is drawn off and collected and then refined in a wooden tar still equipped with a copper steam heating coil and with a copper tubular condenser. The wood oils are recovered by means of this still. The tar residue left in the still is conveyed to the tar storage tank to be used as fuel.

Primary Still.—The liquor in the last of the wooden settlers, which is practically free from tar in suspension, is run by gravity through a copper pipe into a copper primary still, and the feed is continuous and kept so by a float valve. In this still the tar in solution is separated. The still is made entirely of copper and supplied with a copper steam heating coil, copper neck and copper tubular condenser. The tar from the primary still is considered a waste product and is conveyed to the tar storage tank to be used as fuel.

Neutralizing.—The liquor which is obtained by the condensation of the vapor issuing from the primary still and passing through the condenser is conveyed to a wooden neutralizing tub, where it is treated with slaked lime. The tub is provided with an agitator to properly carry on the neutralization.

Lime Lee Still.—The neutralized liquor is carried to a steel still, called a lime lee still, and here the acetate of lime is separated from the wood alcohol. It is equipped with a copper steam heating coil and with a copper tubular condenser. From the lime lee still the process separates into two branches.

Settling Tanks and Steam Pans.—We will first follow the progress of the acetate solution, which is what remains in the lime lee still after the wood alcohol has been driven off in the form of vapor. The acetate solution is pumped or blown with steam or compressed air from the still into steel settling tanks, in which the solid matter precipitates. The solution is then drawn off and piped into steam-jacketted evaporating pans, where the greater portion of the water is evaporated, leaving a substance of consistency which can be handled with an ordinary hand shovel. From these pans the substance, which is acetate of lime, is shoveled out onto drying floors situated above the ovens, and it is spread in a thin layer and allowed to become thoroughly dry. This is now grey acetate of lime of an

average of 80 per cent. and is ready to be placed in bags for shipment.

Drying Floors.—The drying floors are over the tops of the ovens, and are made of tile brick or concrete. They are supported by I-beams or rails and are so designed that they utilize the waste heat above the tops of the ovens.

Weak Alcohol.—Returning to the lime lee still, the vapor which passes off when the contents are heated goes through a tubular condenser and the condensation product, termed weak alcohol, is conveyed into steel tanks, the capacity of which is sufficient to supply one charge for the alcohol still.

Alcohol Still.—The weak alcohol is piped from the tanks just mentioned to a steel alcohol still, equipped with a copper steam heating coil and with a copper fractionating column. Its purpose is to remove the water from the solution and to produce 82 per cent. wood alcohol (called crude alcohol), which is the grade manufactured in most of the wood distillation plants.

Woods and Yields.—The principal kinds of hard woods used in destructive distillation are beech, birch, maple, oak, hickory, red gum and others which are comparatively free from gums, tannins, etc. Any part of a tree can be used down to the branches two inches in dimater. The wood is allowed to season for several months before being carbonized, the idea being to allow nature to remove as much as possible of the superfluous water in the wood. Different kinds of woods yield different quantities of by-products, the average, it is said, being about as follows for each cord of wood: Charcoal, 50 to 60 bushels; acetate of lime, 190 to 240 pounds; 82 per cent. wood alcohol, 9 to 12 gallons. Charcoal weighs approximately 20 pounds to the bushel.

The crude wood alcohol is taken from the alcohol still of the crude wood plants, and shipped to wood alcohol refineries, the principal ones in the United States being located in Buffalo, N. Y., and Newark, N. J. Here the crude alcohol is first pumped into storage tanks, and after careful analysis, showing the amount of alcohol, amount of acetone, and amount of oils present, it is drawn into big iron stills, where it is treated with an amount of caustic soda, sufficient to take care of oils and impurities indicated by the analysis.

After this reaction has had an opportunity to proceed to the right point, it is distilled, the distillate being water-white and gath-

ered in large tanks. This is then drawn into copper stills where it is treated with sulphuric acid to neutralize any alkaline bodies which may have been carried over in the distillation on caustic soda treatment, and is then carefully distilled in column stills.

The first part of the run contains acetone and esters figured as methyl acetate. Methyl acetate is one of those peculiar organic bodies which has a high specific gravity and exceedingly low boiling and volatilizing point. This mixture of acetone, methyl acetate and alcohol, which is first fractionated off, is sold under the trade name of Methyl Acetone, and is used largely as a solvent.

Next is fractionated off that part of the run which is pure alcohol, containing, when carefully watched, less than $^1/_{10}$ of 1 per cent. acetone, and being as near pure chemically into CH_3OH as is possible to obtain. This is the part used by the formaldehyde and dye manufacturers.

The last part of the run, or tailings, so-called by the distiller, contains some very accurate poisonous compounds, and this is the portion used for making denaturing wood alcohol, which is the material specified by the Internal Revenue Department for the denaturing of ethyl alcohol.

Uses of Wood Derivatives.—The chemicals derived from the destructive distillation of hard woods are used as follows:

Uses of Charcoal:

In the manufacture of charcoal pig-iron; in the manufacture of gunpowder; artificial fertilizer; insulator; deodorizer; metallurgical purposes; briquetted fuel; domestic lump fuel.

Uses of Acetate of Lime:

Acetic Acid—For manufacturing acetates, artificial vinegar and in photography, tanning, dyeing, and the curing of skins.

Acetone—For manufacturing gunpowder, chloroform and iodoform; also in the paint trade as a solvent.

Aluminum Acetate—For dyeing, mordanting and waterproofing fabrics.

Chromium Acetate—For mordanting cotton.

Copper Acetate (Verdigris)—Used for oil paints, green colors, artificial flowers, stains for wall paper and for dyeing black on wool.

Iron Acetate—Used for impreganting wood, dyeing black and violet, dyeing and weighing raw silk, and in the manufacture of hats and inks.

Lead Acetate (Sugar of Lead)—In painting, calico printing, loading white silk and in the manufacture of chrome yellow and thirty derivatives therefrom.

Potassium Acetate—In the manufacture of acetic acid and of dehydrating and decomposing agents.

Sodium Acetate—Same as in preceding paragraph.

Uses of Wood Alcohol:

For denaturing grain alcohol, in the manufacture of gunpowder, manufacture of aniline coal tar colors, manufacture of formaldehyde, manufacture of celluloid and moving picture film, and as a solvent for hydrocarbon resins and gums. Shellac made from wood alcohol being very much superior to any other.

So great has become the demand for wood alcohol, and there has been so little increase in supply, that prices have risen in the last few years from 40 cents to 50 cents a gallon to $3.00 to $3.50 a gallon, owing to the grade, and even at these prices it is impossible to supply the demand.

ETHYL ALCOHOL.

Ethyl, or so-called grain alcohol, in which the drug trade are most vitally interested, has been for the past several years, owing to high price of grain, made practically entirely from molasses. The molasses used is what is known in the trade as black-strap molasses, and is the final residue after all the sugar has been crystallized out of the concentrated syrups from whatever source the sugar may come. This molasses is taken to the distilleries in tank steamers, or tank cars, and in some instances by pipe lines, where it is conveyed by pipes into big fermenting tubs.

In these tubs it is mixed with just the right amount of water and yeast, cultured. After fermentation has been allowed to go to just the right point, which an expert can detect by watching the action closely, the mixture is drawn into a big still, known as a beer still. Steam is immediately turned on, and the alcohol in crude forms is distilled over.

This alcohol is then treated, first with alkali, giving primary distillation similar to that of wood alcohol, and then neutralized with acid, and redistilled in a column still.

The first alcohol that comes over has some odor, and is not over 188 proof. The next alcohol is the heart of the runs, which runs 190 to 192 proof, and is entirely free from odor, and is what is known

in the trade as Cologne Spirit. The last of the run develops some odor again, and contains aldehydes which, for many chemical purposes, cause disastrous results.

For pharmaceutical uses and for chemical uses, the heart of the run, or what is known as Cologne Spirit, is all that is fit to use. The first of the run, which is called the heads, and the last, which is called the tails, are mixed together to be used for ordinary denatured alcohol for non-freezing and solvent purposes.

The Internal Revenue Department has permitted a number of formulas of Denatured Alcohol aside from those which are authorized for Completely Denatured Alcohol, that can be sold to anybody. These additional formulas are known as special formulas, and can be bought by any manufacturer who has sufficient responsibilities to secure bond. Bond must be given for the amount of tax that this said manufacturer would be liable to, should this alcohol be misused. In other words, the manufacturer must give bond enough to cover $4.18 a wine gallon for every gallon of alcohol which he uses, or has on hand during a period of 30 days.

A number of these formulas are particularly applicable to pharmaceutical preparations, but it must be definitely understood that they are only to be used for the purpose for which they are specified, and in no instance are they to be resold, except as the finished product for which they are intended.

Since the first of the year, alcohol prices have mounted to the highest levels on record. Sales of spot ethyl alcohol, 190 proof, have been recorded during the past month at figures ranging anywhere from $6.00 per gallon up to $8.00, which prices consumers have been compelled to pay, buying in a resellers' market. For shipment from middle western or southern distilleries, goods have been offered at $5.40 up to $5.75, but with the present railroad situation, the actual time of delivery to the consumers' plants makes this a rather uncertain type of purchase. Contracts in effect between distillers and consumers at the present time are understood to be priced at slightly over $5.00 although a contract is said to be no assurance of obtaining a steady supply of alcohol to-day. The fact that many large users have been forced into the open market to pick up spot alcohol in any way that they have been able, is evidence of the general shortage of supplies.

Causes of Shortage.—In speaking before an association of one of the leading consuming industries in the country, the president of a

large producing corporation said recently that supplies of alcohol all over the United States were far below normal and that he could not see at the time from what source legitimate consumers would be able to obtain sufficient supplies for their needs after the present short holdings are used up. Distilleries using molasses as a raw material have been unable to obtain anything like enough to keep them running at capacity. For those using corn, which is now just under the two dollar mark, the price has become almost prohibitive. Added to this, practically two months of crippled shipping facilities have furnished the crowning feature of the situation by isolating consumers from their sources of supply and holding up shipments of raw materials destined for the distilleries.

The molasses production of Cuba, from whence comes most of that used in this country for the production of molasses alcohol, has been materially curtailed during the past year by strikes. The high price of sugar has also been a factor in the more careful refining which has given a higher sugar return and consequently reduced the molasses output. The market and prices in the United States have been on what is termed a "grain basis" as a result, that is, the cost of alcohol corn has been the determining factor in the price and is expected to be for the balance of this year if not longer. The present price of corn for alcohol (about $1.60 per bushel) means a cost to the producers of 70 cents to 75 cents a wine gallon.

SUGGESTIONS FOR UNITED STATES PHARMACOPOEIAL REVISION SUBMITTED BY THE COMMITTEE ON THE UNITED STATES PHARMACOPOEIA OF THE PHILADELPHIA COLLEGE OF PHARMACY.

MAY, 1920.

(*Continued from p. 563, August, 1920.*)

BIOLOGICAL PRODUCTS AND STERILIZATION.

Aqua Destillata Sterilisata.—Mention should be made here, as under physiological solution of sodium chloride, that an autoclave is to be preferred for its sterilization. When boiling is to be used, the term "actively boil" should be employed, and not merely boil. The statement is made that this preparation should be used within forty-eight hours after it is made. This should be followed by the statement, "if it is to be used for intravenous injections." It is

neither necessary nor practicable to use a freshly prepared product except for intravenous or intramuscular injections.

Liquor Sodii Chloridi Physiologicus.—In the sterilization of this preparation, boiling is permitted for at least one hour, but no mention is made of the fact that if such a process is used, the evaporated water must be replaced by sterilized, freshly distilled water. Such a statement should be inserted, and the operator directed to simultaneously prepare sufficient sterilized, distilled water in a second flask. In stopping the flask, it is desirable to place a piece of sterile gauze under the cotton plug.

The statement is made that this solution should not be used after it has been made forty-eight hours. This should be followed by the phrase, "if it is to be used for intravenous injections."

Why should sterilized distilled water be boiled for one-half hour and this preparation for one hour to insure sterile end products? For the sake of uniformity, the time directed should be the same in each case.

Virus Vaccinicum.—Mention is made that the pulp is rubbed up into a smooth emulsion with glycerin. It might be well to state, "with sufficient glycerin to cause it to conform to the established standard."

Blood Coagulants.—There is a large demand for a good blood coagulant. A method of preparing such a product, together with a method for its standardization should be introduced into the next U. S. P.

Beef Extracts, page 527.—Why should the U. S. P. refer to Liebig's or any other make? It is true that this make is very satisfactory, but the Pharmacopoeia should not name any specific manufacture.

REAGENTS, TEST SOLUTIONS, ETC.

Culture Media.—If retained, a more comprehensive list should be included. Methods for determining reactions or, if advisable, the hydrogen-ion value of these products should be added.

Sterilization.—A page and a half is devoted to the exceedingly interesting and important subject of sterilization. A more intensive and instructive chapter, giving the specific details of procedure should be provided. As it is at present, it is of little value and might as well be deleted.

Staining Solutions.—If retained, mention should be made of Pappenheim's Solution and Aniline Gentian Violet, giving the ingredients and methods of preparation.

Blood Reaction, page 619.—The benzidene test should be introduced.

Urea Estimation, page 620.—The Urease Method for determining urea should be introduced.

Benedict's Solution, page 621.—These solutions for qualitative and quantitative determination of glucose should be introduced. Mention should be made of the fermentation method for the determination of glucose in urine.

Gastric Contents, page 621.—Sahli's reagent for the determination of free acidity should be mentioned, as well as Uffelman's reagent for lactic acid.

Diagnostical Reagents.—If the Revision Committee decides to retain the Diagnostic Reagents in the U. S. P., many other reagents which are at present used in the Newer Blood Chemical Tests should be introduced. In making up such tests, there are also standard solutions for colorimetric comparisons, in addition to reagents, which it is desirable and essential to include in the Pharmacopoeia.

PHARMACODYNAMICS.

The incorporation of the chapter on "Biologic Assays" in the U. S. P. IX is an epoch in the history of standardization and this method of assay should be applied to a greater number of drugs which cannot be satisfactorily assayed by chemical means.

We recommend that more of the methods be made compulsory instead of optional and that biologic assays be included for Ergot, Gelsemium, Lobelia, and Veratrum Viride. We would, however, recommend that these tests be referred to as "Pharmacodynamic Assays" instead of "Biologic Assays", and thus make the Pharmacopoeia conform with the definitions of the Pharmaceutical Syllabus.

As a result of personal experience and the number of papers which have been published criticising the present U. S. P. methods, we are of the opinion that the "Biologic Assay Methods" of the U. S. P. IX are unsatisfactory, due to the fact that in many cases *they lack the details* which workers in the practical laboratory have found essential in order to obtain accurate results. In other words, the methods are in many instances *not as accurate and up-to-date* as the methods in common use at the present time in commercial

laboratories, and therefore do not show as well as they might, the degree of efficiency to which biologic assays have been developed.

Due to this fact, very little attention has been paid to the methods as set forth in the U. S. P. IX, as all evidence tends to prove that they are less accurate and reliable than the methods in common use.

In the second paragraph of the chapter on "Biologic Assays" in the U. S. Pharmacopoeia, the following statement appears:

"Brief descriptions of the more commonly accepted methods are given here in order, first, to direct the attention of manufacturers to them; second, to ascertain the points of weakness which may exist in them; and, finally, to outline methods and establish standards which those interested may adopt should they desire to assay their products and have them conform to the standards proposed."

For the reasons stated above, remarks are mostly limited to what we consider "points of weakness" which exist in the present U. S. P. methods.

Cannabis, page 605.—"Before administration the animal should not be fed for twenty-four hours in order to hasten absorption."

It is not necessary to withhold food for more than ten to twelve hours before making a test, as the stomach will be completely emptied in this time and it will not be so hard on the animal.

"The head of the animal being held, its mouth is opened and the capsule or pill is placed upon the back of the tongue. Usually the drug is easily swallowed when given in this way, but this may be facilitated by giving the animal a small amount of water to drink."

This method works sometimes, but as a general rule the dog does not feel inclined to take the capsule so easily. In practical work it will be found that it is almost impossible to make the dog swallow a capsule by the above method. Pulling the tongue well forward, placing the capsule far on the back of it and then releasing the tongue, is an improvement, but the best method is the following:

"Open the animal's mouth by forcing the thumb and index finger of the left hand between the jaws, back of the teeth. The capsule is then placed on the back of the tongue with the right hand and the mouth quickly closed; while still holding the mouth shut, the animal can be made to swallow the capsule immediately by slapping it on the throat."[1]

By this method the most obstinate dog can be made to swallow the capsule on the first attempt.

[1] Pittenger: "Biochemic Drug Assay Methods," page 101.

In lieu of a standard extract furnished by some central authority such as the U. S. Hygienic Laboratory, what is the use of running an assay each time on a standard preparation when the strength of the standard is obtained by adjusting a preparation until it is of such strength that 0.03 Mil. of the fluid extract per kilo will produce incoördination.

Why not adopt 0.03 Mil. per kilo as a standard and calculate the strength of the unknown by comparing the dose of it necessary to produce incoördination with the above 0.03 Mil. per kilo instead of the amount of the standard necessary to produce the same effects? If the standard is of proper strength, will it not require exactly 0.03 Mil. per kilo? The only object for assaying the standard preparation each time would be to avoid errors due to the variation in the susceptibility of dogs. The use of a standard preparation, unless supplied by some central authority, will not avoid this error because the standard preparation is adjusted to the above *standard dose* and not to *standard dogs*. Are you not just as liable to have dogs which are over or under normal susceptibility when you adjust the standard as when assaying an unknown, thus making the standard slightly over or under strength? If so, by adopting the longer process of assaying both standard and unknown each time, the error due to variation in susceptibility is only increased because you adopt as a standard preparation one which may be slightly over or under strength and then adjust all subsequent preparations to this, thus making the same error in all, whereas by the shorter method of adopting a definite dose as standard we only have an occasional preparation a little off strength, due to an over or under susceptibility of the dogs used on that particular assay.

Due to the variation in susceptibility of different dogs, the method must essentially be comparative and not absolute. This necessitates the adoption of an arbitrary standard with which the activity of the unknown can be compared. The U. S. P. method would, therefore, be very satisfactory had the Committee only gone a step farther and, as suggested by Pearson,[1] made arrangements for supplying manufacturers with a suitable standard with which to compare the activity of their preparations. Until such a standard is supplied, however, it is only a waste of time to run an assay on a standard preparation, *which the manufacturer has prepared himself;* each time an unknown sample is tested.

[1] Pearson, THIS JOURNAL, Nov., 1916.

Some workers have objected to the standards adopted by the Pharmacopoeia for Cannabis, claiming that they are too high. Personally we have found no difficulty in meeting the U. S. P. requirements for preparations of Cannabis.

The method of stating the standard, however, is open to criticism. The U. S. P. states:

"When assayed biologically Fluid extract of Cannabis produces incoördination when administered to dogs in a dose of not more than 0.03 Mil. per kilogram of body weight."

According to the above statement, a dose larger than 0.03 Mil. per kilo would not produce incoördination. The words "not more than" should either be omitted or changed to "in a minimum dose of 0.03 Mil. per kilo."

Some workers have objected to the action of the Committee in making the test for Cannabis compulsory because it is one of the least satisfactory of the pharmacodynamic tests, and would, therefore, be a hardship on the retail druggist in that he would be held accountable for the activity of his Cannabis preparations when only an expert could satisfactorily carry out the test.

This criticism would be justified had the Committee adopted a standard reading "the minimum dose of Fluid extract of Cannabis necessary to produce incoördination should be *not less than* — Mils per kilo, nor more than — Mils. per kilo."

The standard adopted, however, only specifies a *minimum* activity in order to guard against fraudulent, inert or badly deteriorated drugs and does not specify "limits" as in the chemical assays for alkaloidal drugs.

No hardships are imposed upon the inexperienced operator, therefore, because it is only necessary that Cannabis preparations possess a certain minimum activity and it is not compulsory that they actually be standardized.

Unlike most chemical assays, the assay for Cannabis is such that a preparation which passes the inspection of an inexperienced operator is more active than one passed by the expert because the expert can notice marked signs of incoördination in dogs before the first signs are appreciable to the inexperienced.

Of course, the expert is better qualified to actually standardize these preparations, but, as before stated, a person need not be an expert in order to determine whether or not a particular prepara-

tion of Cannabis conforms to the requirements of the U. S. Pharmacopoeia.

Aconite.—The proposed "time limit" of twelve hours is very objectionable as this means twelve hours after the pigs are injected. When you add to this the time of weighing animals, preparing solutions for injections, making injections, etc., the test consumes thirteen hours, which cannot be included in the ordinary working day and makes a rather long week for men employed in laboratories which run these assays almost daily. We would suggest a twenty four hour "time-limit."

Pittenger, by recording the results obtained by using twenty-three and twenty-four hours as a "time limit," proved that the most concordant results are obtained by using twenty-four hours as the "time limit." We do not doubt that a twelve-hour method would be just as accurate as the twenty-four hour method, but it is very objectionable for the reason stated.

We recommend that Gelsemium and Veratrum also be assayed by the Guinea Pig Method.

We cannot too strongly recommend that the biologic assay for Aconite be made compulsory instead of the chemical assay, for while we agree that the chemical assay is a very accurate determination of the alkaloidal content of Aconite, it is not nearly as good an index of the *therapeutic* value of the drug or its preparations, as the pharmacodynamic test, as it has been definitely proven by many workers that the results of the present chemical assay do not parallel the therapeutic activity of the drug.

In other words, it often happens that a preparation of Aconite will run high in the chemical test and low in the physiologic test, due to the fact that a chemical assay does not express the true activity of the drug because it also estimates other alkaloids of lower activity than Aconitine.

This discrepancy between the two tests is easily understood when the nature of Aconitine is considered and it is realized how the acetyl and benzyl groups are split off, thus reducing the physiologic activity of the product without destroying its alkaloidal nature, and allowing it to still be estimated as an alkaloid in the chemical assay process.

The present Pharmacopoeia makes the chemical test compulsory and at the same time recommends that the drug be assayed by the pharmacodynamic method. For the reason stated above, it is

impossible to standardize the product by both methods when the results obtained by one do not parallel those obtained by the other.

We therefore recommend that the pharmacodynamic test be made compulsory in place of the chemical test, or that a double standard, *i. e.*, a chemical standard within a certain range to guard against excessive toxicity and also a minimum biologic standard (a M.L.D.), to guard against inactive or deteriorated preparations be adopted and that preparations which do not conform to both standards be rejected.

Digitalis-Strophanthus-Squill.—The principal criticism of the method as given in the Pharmacopoeia is in regard to the technique as recommended for injecting the doses into the frogs.

The U. S. P. states:

"After the frogs have been weighed as described, the doses to be given are calculated according to their weights and are *measured into small conical glasses by means of a finely graduated pipette.* The doses of the preparation which are to be injected should be as uniform in quantity as possible and *should not exceed 0.015 Mil. for each gram of body weight of frog.* . . . . When the doses are ready, they may be injected into the anterior lymph sac of the animal. This is done by means of a *glass pipette* which is drawn out to a fine point. The frog is held on its back in one hand and the pipette with the contained drug in the other, the mouth of the frog is opened with the point of the pipette and, carefully avoiding the tongue, the floor of the mouth is punctured and the point of the pipette is then seen to enter the anterior lymph sac of the frog. The contents of the pipette are now forced into the sac either by gravity or by gently blowing, if necessary. In the latter case, care should be taken not to introduce air into the sac."

It is *absolutely impossible* to obtain accurate results if this technique is followed. It will be noted that the average frog should weigh 20 Gm. and that the dose injected should not exceed 0.015 Mil. for each gram or 0.3 Mil. for a 20 Gm. frog. You are directed to measure this 0.3 Mil. by means of a *finely graduated pipette* into a conical glass. This *very small dose* (0.3 Mil.) is then sucked up into another *sharp-pointed pipette* and forced into the lymph sac by blowing.

The error due to the amount of solution left in the conical vessel and the second pipette is indeed great when compared with the very small dose given.

The use of the second pipette and the conical glass vessel is no doubt recommended because it is impossible to force the preparation into the lymph sac by blowing and at the same time accurately measure the dose to the hundredth of a Mil.

The two pipettes and the conical glass vessels should be replaced by an all-glass or Record Tuberculin Syringe, which is graduated in hundredths of a Mil. By the use of one of these syringes the *actual amount of the preparation injected* can be measured to the hundredth of a Mil., whereas by the U. S. P. method we only know the amount of solution placed in the conical vessel and not the amount actually injected.

On page 608, first line, the directions state:

"The dose thus found is then compared, etc."

The text fails to state which dose is the *dose* to be compared. It is not stated anywhere that the smallest or minimum dose necessary to bring about the end reaction is the one to be used in computing the strength of the preparation. In other words, the directions give no definite outline for carrying out the tests, but take it for granted that the operator understands the technique of giving the doses in series, progressively increasing or decreasing until the M.L.D. or M.S.D. is found, etc.

Suprarenal Gland.—As stated by Hamilton,[1] "the biologic assay of products of the suprarenal gland is open to criticism in only two particulars, *i. e.*, in the method of measuring and administering the doses and in attempting to check the results as described."

"Using both femoral veins for injecting sample and standard is to obviate the possible mixing of the two solutions if both are injected into the same vein. But it introduces a very much greater source of error. The amount injected can much more easily be measured by use of a pipette than in a syringe, and the dose after being injected can be easily and completely washed into the blood stream by a follow-up injection of 2 Mils. of physiologic salt solution. When this procedure is followed, no mixing of two injections is possible."

Another very good method is to *expose the saphenous vein at its junction with the femoral.* When giving injections, the needle of an all-glass syringe is inserted far enough through the saphenous vein to allow the point to project directly into the blood stream in the femoral vein. After injecting the preparation, the needle can be

[1] Hamilton: "Biological Standardization," THIS JOURNAL, February, 1917.

withdrawn and the saphenous vein clamped with a bulldog clamp The preparation thus injected is entirely carried into the circulation by means of the main current of blood in the femoral vein.

The "checking of an assay by making injections of the sample and of the standard into opposite sides from the first used is no check except in so far as it checks conditions on the two sides of the dog. This feature can better be eliminated by using only one side. Further, by the official method, if it is impossible to complete the test and the check on a dog, no option is left, but to repeat both test and check on another dog. It is occasionally necessary to check an assay on a second dog when conditions during the first test were unfavorable to accuracy but no advantage results from a retest on the same dog."

Pituitary Extracts.—We strongly recommend that the Isolated Uterus method be retained as the official method for testing Liquor Hypophysis.

Several papers have been written recommending the blood pressure method, but our experience has been that the isolated uterus method is the best so far proposed, as differences of activity which are only just appreciable by the blood-pressure method, under the best conditions, are at once obvious in the test on the uterus without any special care in controlling the regularity of the response.

We are of the opinion, however, that more concordant results can be obtained by employing the *whole* one horn of the uterus of a 350 to 425 Gm. pig as suggested by Pittenger,[1] instead of only a *segment* of the one horn of the uterus of a 250 Gm. guinea pig; also by controlling the contractions of the uterus by means of an escapement wheel and bucket for holding shot instead of the small heart lever recommended. When the whole horn is used, the heart lever is not heavy enough to allow sufficient weight to be added to control the contractions of the muscle.

The assay for Liquor Hypophysis requires more experience on the part of the operator than any other biologic test in the Pharmacopoeia, and, although compulsory for a U. S. P. product, it is not included in the chapter on "Biologic Assays."

Under "Liquor Hypophysis," however, we find that the product must be tested "as directed by the United States Hygienic Labora-

[1] Pittenger: "An Improved Apparatus for Testing Drugs upon the Isolated Uterus," *Jaur. A. Ph. A.*, June, 1918.

tory." We would recommend that the complete details of this test should be included in the U. S. P.

The principal criticism of the U. S. P. method for testing Liquor Hypophysis, however, is not with the method itself but with the standard adopted.

Before readopting a complex substance like Beta-aminazolyl-ethylamine Hydrochloride as a standard for adjusting the strengths of commercial preparations, a thorough study of the following points should be made:

1. Degree of uniformity in the physiologic action of different available samples of the proposed standard substance.
2. Rate of deterioration of solutions of this substance.
3. Effect of sterilization on solutions of this substance.
4. Rate of deterioration of the substance itself.
5. Effect of repeated doses on uterus.
6. The toxicity of the substance as compared with Pituitary Extract.
7. The relative toxicity of a Pituitary Extract of the strength proposed by the U. S. P. IX and that of the commercial extracts as supplied by the leading pharmaceutical manufacturing houses.

The standard adopted by the U. S. P. IX is very low, it having been shown by comparison that the commercial extracts prepared by the leading pharmaceutical houses, which have had preparations on the market for several years and with which the physicians have become accustomed as to dosage, etc., are from three to five times as active as an extract of the U. S. Pharmacopoeia standard strength. This is unfortunate, as there is no reason why a weaker preparation than the one to which physicians have become accustomed should be placed on the market.

It is hoped, therefore, that if this substance is retained as the standard test substance, definite requirements as to its purity and uniformity of activity can be drawn up, and that an accurate co-ordination of the required U. S. P. strength and of the common pharmaceutical practice may be secured.

DRUG ASSAY

The methods given in the U. S. P. for drug assays are generally quite satisfactory and there are but a few alterations necessary. The chapter on proximate assays in Part Two is particularly to be commended, as it is clear, complete and informative. The errors

found are merely those of phraseology; for instance, in the first paragraph on page 593 it is stated that alkaloids "are more or less soluble in alcohol, chloroform, ether, amyl alcohol, benzene, petroleum benzin, or mixtures of several of these." The latter phrase is somewhat misleading, as it conveys the impression that the alkaloids are not soluble in a mixture of two of the solvents but only in a mixture of more than two, or, in other words, of several. In our opinion, the latter part of this sentence should be changed to read as follows: "More or less soluble in alcohol, benzene, petroleum benzin, or a mixture of two or more of these." The same sort of error occurs in paragraphs three and four, page 594. In paragraph three it is stated that a mixture of *more* than one volume of chloroform to one volume of ether will separate in the bottom of the separator. As a mixture of equal volumes of chloroform and ether is also heavier than water, the sentence should read as follows: "A mixture of one volume or more of chloroform to one volume of ether will settle in the bottom of the separator." The correction of paragraph four is of the same order, as the phrase should read: "Two volumes or more of ether to one volume of chloroform."

Indicator.—It is recommended that *methyl red* be specifically directed for use in the various assay processes instead of cochineal. Methyl red gives clear end-points in all cases, whereas the end-point with cochineal, when assaying aconite, ipecac, nux vomica, or opium, is rather obscure and difficult to determine. Cochineal could be permitted for alternate use as methyl red now is.

Detection of Alkaloid.—On page 594, in paragraphs five and six, under the instructions for determining the presence or absence of alkaloid during the various stages of the assay, it is stated that the solution tested should show not more than a very faint cloudiness on the addition of a drop of mercuric-potassium iodide T. S., or in the case of caffeine or colchicine on the addition of a drop of iodine T. S. Experience has shown that it is necessary to "shake out" until a negative test has been obtained, particularly in the case of extracts, such as powdered and solid extracts of belladonna leaves, which require more than the usual number of shake-outs. Ordinarily, and particularly in the case of crude drugs, three or four shake outs are sufficient to extract all of the alkaloids, but in the case of the belladonna and other extracts many more shake outs are

usually needed to extract all of the alkaloid. A faint cloudiness may be obtained after each of a number of extractions, due probably to the difficult solubility of the alkaloid. In the aggregate, the alkaloid extracted by each of these shake-outs represents a substantial quantity, particularly if the lot being assayed is a large one. In view of these facts, we recommend that the words, "not more than a very faint," as found on lines twenty-six and thirty-nine (page 594) be omitted and the word "no" substituted so that the phrase shall read: "Shows no cloudiness on the addition of."

Determination of Alcohol-Soluble Constituents.—A standard method for the determination of the alcohol-soluble constituents of asafoetida, benzoin, gambir, gamboge, kino, and myrrh is needed. A continuous extraction method is recommended because of its ease of operation and the saving of time and solvent. As some of the constituents dissolve rather slowly a test should be included to determine if the extraction is complete.

Menstrum for Assay of Crude Drugs and Extracts.—Considerable trouble has been experienced with the menstrum composed of ether, two parts, and chloroform, one part, which is directed to be used as the macerating medium, in various assay processes, as given under belladonna root. An ether chloroform mixture in these proportions is not satisfactory on account of a strong tendency to form emulsions. Complete contact of all portions of the two layers of liquid is quite difficult and much more time is required on account of the necessity of using much care during the agitation. The disintegration of emulsions is also time consuming, so that this factor, together with the other factors, previously stated, renders it necessary to change the proportions of ether and chloroform used as menstrum or solvent. The menstrum of three parts of ether and one of chloroform, as used in the U. S. P. VIII, is much more satisfactory as it permits a more vigorous agitation and a complete contact of the two layers. A menstrum composed of these proportions of ether and chloroform is much less likely to form emulsions and gives a cleaner separation of the two layers. We therefore earnestly recommend the re-adoption of the menstrum of ether, three parts, and chloroform, one part, as formerly used in the U. S. P. VIII.

Assay of Fluid and Solid Extracts and Tinctures.—The assay of solid extracts of belladonna, hyoscyamus, and stramonium could be simplified and shortened if a maceration method, such as that used for powdered extracts were adopted. The present method of dis-

solving the extract in dilute alcohol and transferring directly to a separator, gives considerable trouble, on account of the formation of emulsions, which is partly due to the unavoidable presence of undissolved matter. Instead of a direct shake-out, we recommend that the extract be dissolved in a suitable solvent, spread over oak sawdust, evaporated at a low temperature, transferring to a flask and treating in the manner described for powdered extract of belladonna. Similar methods could be used for fluid extracts of belladonna, guarana, hydrastis, hyoscyamus, and nux vomica, and also tinctures of belladonna, hydrastis, hyoscyamus, nux vomica, and stramonium. At present the maceration method is used for fluid extracts of aconite, cinchona, ipecac and pilocarpus and tincture of aconite, cinchona, and physostigma. The application of the maceration method would decidedly lessen the danger of emulsification and requires a fewer number of shake-outs to extract the alkaloid.

Physostigma.—The U. S. P. method for the assay of this drug and its preparations has been found to give erroneous results. Low results have been consistently obtained and are probably caused by the heat used in the assay, and to some extent by incomplete extraction. As a substitute method we offer for consideration the method devised by Mr. George E. Ewe, which was published in the December, 1919 number of the *Journal of the American Pharmaceutical Association*. This method eliminates most of the heating and has given satisfactory results in the H. K. Mulford laboratories.

CONCENTRATED MILK PRODUCTS.*

By J. W. England,

PHILADELPHIA, PA.

CONDENSED MILK.

Condensed milk is an evaporated milk representing about two and a half times its volume of fresh milk and containing about 40 per cent. by weight of cane sugar. It is a of thick syrupy consistency and very sweet taste, and is marketed in cans. Commercially, it is made by dissolving cane sugar in fresh milk by a warming pan, after which it is drawn into the vacuum pan where it is condensed

* Read before the annual meeting of the Pennsylvania Pharmaceutical Association, held June, 1920.

at a temperature of 120° to 130° F. until the volume of liquid is 40 per cent. or less of the original volume; if the milk be overheated, the albumin will be coagulated and the sugar caramelized. After condensation, the milk is drawn off into cooling cans and constantly stirred in a sanitary room and atmosphere for two or three hours until a temperature of 70° F. is reached, when it is quickly canned and sealed.

Some of the more modern canners of milk, sterilize the cans with dry heat before filling them, but the cans are cooled *in vacuo* before being filled, otherwise the milk congeals. If the milk condensed be acid, a certain amount of invert sugar (dextrose and levulose) is formed. Some manufacturers use invert sugar in place of cane sugar (U. S. D. 20 Edt., 1498), because invert sugar has a less sweet taste than cane sugar and is less liable to cause sugar of milk to crystallize in the can.

According to Food Inspection Decision No. 170 (U. S. Department of Agriculture, March 31, 1917), condensed milk must be the product of the evaporation of whole, fresh, clean cow's milk and must contain at least 8 per cent. milk fat and not less than 28 per cent. total milk solids.

Condensed milk is not sterile and may contain pathogenic organisms; it is preserved against decomposition by its high percentage of sugar, which also prevents freezing during transportation. So long as the can is unopened, condensed milk will keep under favorable conditions for a year or two, but after several months it becomes darker in color and thicker; when the can is opened, if kept in a cool and sanitary place, it will keep for several days.

Condensed milk was the first form of canned milk put on the market. "The early French inventors along this line, dating back over a hundred years, are said to have been called forth by Napoleon's efforts to obtain a milk that could be transported for the use of his armies. It is interesting to note that canning milk first became a successful enterprise because of the urgency in this country of feeding the soldiers of the North in the Civil War." ("Condensed Milk and Milk Powder:" Otto F. Hunziker. Published by the author, Lafayette, Ind., 1914.)

During the recent World War, the demand for condensed milk was enormous. Mr. Charles E. Hires, of Philadelphia, one of the leading manufacturers of condensed milk in the country, writes me as follows:

"Following the thought expressed by you yesterday relative to the production of condensed milk in the United States, it gives me pleasure to enclose herewith the data of same:

I do not have an accurate record of the amounts produced in 1914 and 1915, but the amounts exported were as follows:

	Pounds.
1914	22,850,904
1915	75,689,584

The amounts manufactured and exported were as follows:

	Pounds.	Pounds.	Percentage Exported.
1916	992,364,000	219,686,127	22
1917	1,333,787,000	428,575,213	32
1918	1,675,934,000	551,139,754	33
1919	2,030,958,000	852,865,414	42

The number of cases of condensed and evaporated milks manufactured were as follows:

1916	Condensed	5,931,000
	Evaporated	14,474,000
1917	Condensed	7,482,000
	Evaporated	19,618,000
1918	Condensed	10,188,000
	Evaporated	22,998,000
1919	Condensed	13,441,000
	Evaporated	25,720,000

I believe these figures to be reliable. The data was compiled by The National Canners' Association of Washington, D. C."

"Milk," an exceedingly informative pamphlet issued by the U. S. Department of Labor, Childrens' Bureau, No. 35, 1918; written by Dr. Dorothy Reed Mendenhall, and from which considerable data in this article have been taken, gives the following average percentage composition of condensed milk:

AVERAGE COMPOSITION OF CONDENSED MILK (HUNZIKER).

Fat	9.0
Protein	8.5
Milk sugar	13.3
Cane sugar	40.9
Ash	1.8
Water	26.5
	100.0

One of the best known brands of condensed milk, can marked "net weight 15 ounces," has upon its label the following statement: "By adding 1 part of water to 1 part of the contents of this can, a resulting milk product will be obtained which will not be below the legal standard for whole milk." Presumably, *parts by volume* are meant—not parts by weight. On examining this condensed milk, I found it had a specific gravity of about 1.26 and one tablespoonful (rounded) weighed about 350 grains. (The tablespoon is the usual form of measurement for the smaller dilutions.) Therefore, one tablespoonful of the condensed milk mixed with one tablespoonful of water represents, practically, 60 per cent. by weight of condensed milk; with 6 tablespoonfuls of water represents 20 per cent. by weight; with 12 tablespoonfuls of water represents 11 per cent. by weight; with 18 tablespoonfuls of water represents 8 per cent. by weight. With these factors the percentages of the food elements in the different dilutions when measured by the tablespoon can be readily ascertained.

But the tablespoon "heaps" when filled with condensed milk, measuring more than 240 minims (as with water). Hence, one fluid ounce of condensed milk (S. G. 1.26) weighs about 575 grains and mixed with an equal volume of water represents, practically, 56 per cent. by weight of condensed milk, with 6 fluid ounces of water, represents 17 per cent. by weight, with 12 fluid ounces of water represents 9.5 per cent. by weight, and with 18 fluid ounces of water represents 6.5 per cent. by weight.

In making condensed milk dilutions for infant feeding, the graduated measure should be used instead of the tablespoon; it is much more accurate.

Condensed milk is often useful for feeding infants, but it has its limitations. It "is advisable for temporary use during attacks of indigestion, for infants with feeble digestion, especially in summer, for very young infants during the first two or three months, or among the very poor when the cow's milk which is available is still more objectionable" (Holt), and also for undernourished infants where the use of a rapidly assimilable body fuel like sugar is indicated. In traveling, it is most convenient as well as the safest food to use. It is usually diluted six times or more with water, according to age. But condensed-milk-dilutions are illy-balanced, physiologically, containing low percentages of fat and protein and a high content of sugar, and hence, even if prepared under the best possi-

ble conditions, "should not be used as a permanent food when good fresh cow's milk can be obtained" (Holt).

The composition of human milk averages fat 3.5 per cent., protein 1.5 per cent., and sugar 7 per cent.; cow's milk averages fat 4 per cent., protein 3.5 per cent., and sugar 4.50 per cent. The U. S. (Federal) minimum standard for cow's milk is fat 3.5 per cent., non-fatty solids 8.5 per cent. (U. S. D. 20th Edit., 1918, 1498).

EVAPORATED MILKS.

Evaporated milk, formerly mis-named evaporated cream, is an evaporated milk representing from two to two and a half times its volume of fresh milk and containing no cane sugar. It is an unsweetened condensed milk. It has the consistency of thin cream and is much less sweet than condensed milk. It is sold in cans and in many large cities is delivered fresh daily in bulk.

Commercially, it is made by evaporating fresh milk *in vacuo* until the volume of liquid is from 40 to 50 per cent. of the original volume, placing it in cans and then sterilizing the contents by subjecting the cans to steam under pressure. The temperature must be "high enough and maintained long enough to insure absolutely sterility to the product and to give the milk sufficient body to prevent the separation of the butter fat in subsequent transportation and storage." ("Milk," U. S. Department of Labor, Bulletin Publication No. 35, 1918.)

The Federal regulations require that evaporated milk must be made from whole, fresh, clean cow's milk and must contain at least 7.8 per cent. fat and not less than 25.5 per cent. total milk solids (Food Inspection Decision No. 158, U. S. Department of Agriculture, April 2, 1915). It will be noted that the standard required for milk solids in evaporated milk is nearly the same as that for condensed milk.

Evaporated milk is, or should be, absolutely sterile and will keep almost indefinitely so long as the can is unopened; once opened, however, it rapidly decomposes (but does not sour first, like condensed milk, it putrefies); it should be kept well iced and used in a day or two.

Chemical Age (June, 1920, 188) states that: "As a matter of more than passing interest it should be noted that evaporated milk, part or full skimmed, modified with foreign fat or vegetable oils, has been used in increasing quantities as a substitute for true

evaporated milk for home consumption. While but 12,000 pounds were tinned in 1916, more than 62,000,000 pounds of the case goods were manufactured in 1919, as shown by the following table. In 1916, the production of the substitute compared with the production of true evaporated milk, case goods, was negligible, while the production had increased to over 5 per cent. by the close of 1919:

PRODUCTION (IN POUNDS) OF EVAPORATED MILK (PART OR FULL SKIMMED) MODIFIED WITH FOREIGN FAT IN THE UNITED STATES, 1916–1919.

Year.	Case.	Bulk.	Total.	Increase Over Previous Year. Per cent.
1916	12,000	14,134,712	14,146,712	...
1917	18,504	17,487,064	17,505,568	24
1918	41,033,855	7,591,182	48,625,037	178
1919	62,262,221	2,748,120	65,010,341	34

"Milk" (1918, 20) gives the following average percentage composition of evaporated milk:

AVERAGE COMPOSITION OF EVAPORATED MILK (HUNZIKER).

Fat	8.3
Protein	7.5
Milk sugar	9.7
Ash	1.5
Water	73.0
	100.0

Dr. D. R. Mendenhall states that "from the feeding experiments recently conducted on animals it does not seem probable that either of the vitamines so far determined is injured by the high temperature. By diluting with equal parts of sterile water, evaporated milk can be reconstituted, approximately, as ordinary milk; also, it can be of great use in the general nutrition of the household and it certainly has a more tenable place in the feeding of infants and young children, when fresh milk cannot be obtained, than condensed milk. We must recognize the facts that it will freeze and is, therefore, not suitable for transportation in cold weather; that it must be carefully handled after opening the can, if it is to remain a sterile food and one fit to give an infant; and that even though condensed to one-half to two-fifths of its original bulk, it is still bulky to transport. Also, all condensed milk is relatively high in price as compared with grade A, raw milk * * * * . All these reasons make evaporated milk far from the ideal substitute for fresh milk."

Dr. L. Emmett Holt ("Diseases of Infancy and Children," 1916, 159) states that: "Evaporated milk requires the same modification (for infant feeding) as ordinary cow's milk. For routine use, it should be diluted with from eight to twelve parts of water and sugar added. * * * * It is a sterile cooked milk. Some children thrive upon it who cannot so well digest either raw milk of the same percentage composition or even freshly pasteurized milk. It should not be continued as the sole food when good fresh cow's milk can be obtained."

One of the best known brands of evaporated milk, can marked "net weight 1 pound," has upon its label the following statement: "By adding one part of water to one part of the contents of this can, a resulting milk product will be obtained which will not be below the legal standard for whole milk. Presumably, *parts by volume* are meant, not parts by weight.

On examining this evaporated milk, I found that it had a specific gravity of about 1.07, and one tablespoonful weighed about 256 grains. Therefore, one tablespoonful of the evaporated milk mixed with one tablespoonful of water represents, practically, 53 per cent. by weight of evaporated milk; with 6 tablespoonfuls of water represents 15.75 per cent. by weight; with 12 tablespoonfuls of water represents 8.5 per cent by weight; with 18 tablespoonfuls of water represents 6 per cent. by weight.

With these factors, the actual percentages of the food elements in the different dilutions measured by the tablespoonful can be readily ascertained.

Evaporated milk does not "heap" on the tablespoon like condensed milk and, therefore, does not bulk so large. One fluid ounce of evaporated milk (sp. gr. 1.07) weighs about 488 grains and mixed with an equal volume of water represents, practically, 51.7 per cent. by weight of evaporated milk, with 6 fluid ounces of water represents 15 per cent. by weight, with 12 fluid ounces of water represents 8 per cent. by weight, with 18 fluid ounces of water represents 5.5 per cent. by weight.

In making evaporated milk dilutions for infant feeding, the graduated measure should be used instead of the tablespoon; it is more accurate.

DRIED MILKS.

Dried milk is milk deprived of its water, or the milk solids, and represents about eight times its weight of milk. It is a yellow.

fluffy powder that is readily miscible with water, forming a milk-like liquid having a cooked milk taste. Dried half-cream milk is similar but is made of milk from which one-half the cream has been removed, and is a light yellow, fluffy powder. Dried skim milk is made from skim milk and is a yellowish white, granular powder.

Commercially, according to "Milk" (1918, 21), milk powder is made by one of the following processes: (1) By feeding the milk in a thin stream over two steam heated cylinders or drums, about one-eighth inch apart, revolving in opposite directions. The milk exposed to the heat of the cylinders dries as a thin film and comes off the revolving cylinder as a sheet, which is easily crushed into a fine powder. The cylinders which are some 60 inches long and 24 inches in diameter are charged with steam under two or three atmospheres of pressure, causing the heating surfaces to have a temperature of about 250° to 280° F. This process, known as the Just patent in the United States and as the Just-Hatmaker patent in England, is said to have been the invention of J. R. Hatmaker of London; (2) by pasteurizing milk and then condensing in the vacuum pan, at a low temperature (130° F.), to about one-fourth its bulk, after which the condensed product is forced under high pressure through minute openings in a metal disk into a hot air chamber. The atomized liquid surrounded by a current of hot air instantly dries and falls to the bottom of the chamber as a snowy powder, the moisture rising as a cloud of steam. The mixture of the liquid and air in the evaporating chamber is stated to be about 180° F. The method was developed in France and is called there and in England the Bevenot de Neveu process. In this country it is known as the Merrell-Gere process; (3) by condensing milk to approximate dryness in a vacuum pan equipped with a mechanical stirrer.

The Federal regulations (Food Inspection Decision No. 170), U. S. Department of Agriculture, March 31, 1917), require that dried milk must contain "not less than 26 per cent. milk fat and not more than 5 per cent. of moisture." There are no Federal standards, apparently, for dried half-cream milk and dried skim milk, except that the latter "shall not contain more than 5 per cent. of moisture."

Dried milk and dried half cream milk are sterile and in sealed cans keep almost indefinitely. Exposed to air, warmth and moisture, however, they slowly become rancid; dried skim milk, however,

with its low content of fat, remains unchanged longer. The dried milks should be stored in a cool and dry place.

Eric Pritchard (*Medical Press and Circular*, Vol. 97: 192–195 (Feb. 25) 1914) gives the following as the average percentage composition of the dried milks:

	Casein.	Albumin.	Sugar.	Fat.	Calories per Oz.
1. Dried milk.....	24.50	1.94	38.92	28.00	146
2. Dried half-cream milk....	30.58	2.42	39.70	15.10	119
3. Dried skim milk.....	31.40	2.49	55.00	1.00	104

The dried milks are now made upon a very large scale and find different uses according to kind. They are used in manufacturing confectionery, such as milk chocolate, baked food products and ice cream, etc., and should find a ready application for soda fountains and in the household. Their utility in traveling is obvious. They possess many advantages—sterility, stability, convenience and cheapness.

Dried half-cream milk is used for infant feeding, more especially in France and England, being similar in such application to evaporated milk. Two ounces by weight mixed with sufficient hot (not boiling) water to make 1 pint, gives a liquid that, except for deficiency in fat, approximates the composition of cow's milk, as follows: Fat 1.5 to 2 per cent., protein 4 per cent., sugar 5 per cent. Dried whole milk mixtures are used, also, for infant feeding, especially for infants over six months of age.

Dried skim milk is used in making bread, rolls, muffins, cakes, custards, creamed soups, sauces and vegetables, cocoa and chocolate; if richer products be wished, the dried milk or dried half-cream milk is employed.

THE MEDICAL DIVISION OF THE NATIONAL MUSEUM.

By Charles G. Merrell,

cincinnati, o.

Those of you who have kept in touch with the proceedings of the American Pharmaceutical Association will recall that some years ago an effort was made to bring about the establishment of a national pharmaceutical museum at Washington, where material bearing upon pharmaceutical history might be collected and deposited for future reference.

The Historical Section of the American Pharmaceutical Association has, for years, busied itself with the collection of historical material of various kinds, and it was largely with a view to providing a permanent home for such material that the movement for a national depository for matters of historical interest from a pharmaceutical standpoint was carried on.

This end has at last been achieved through the enlargement of the field of the Smithsonian Institution, which now, under the name of the National Museum, has established a very interesting medical division, which includes much matter of interest to pharmacists.

This medical division is located on the south side of the gallery in the East Hall of the Arts and Industries Building of the Museum

The subjects illustrated are grouped under four heads, namely:

(1) History of Medicine.
(2) Materia Medica.
(3) Pharmacy.
(4) Sanitation and Public Hygiene.

Three alcoves are devoted to the history of medicine, starting from the beginning of medicine in India, Egypt, Greece, Rome, China, and among the Hebrews.

Two alcoves are devoted to the history of medicine in America, which is illustrated by biographical sketches, portraits, etc.

Three alcoves are devoted to materia medica, and two to pharmacy, including both modern and historical pharmacy. It was through the efforts of Mr. F. L. Lewton that the section of pharmacy was established.

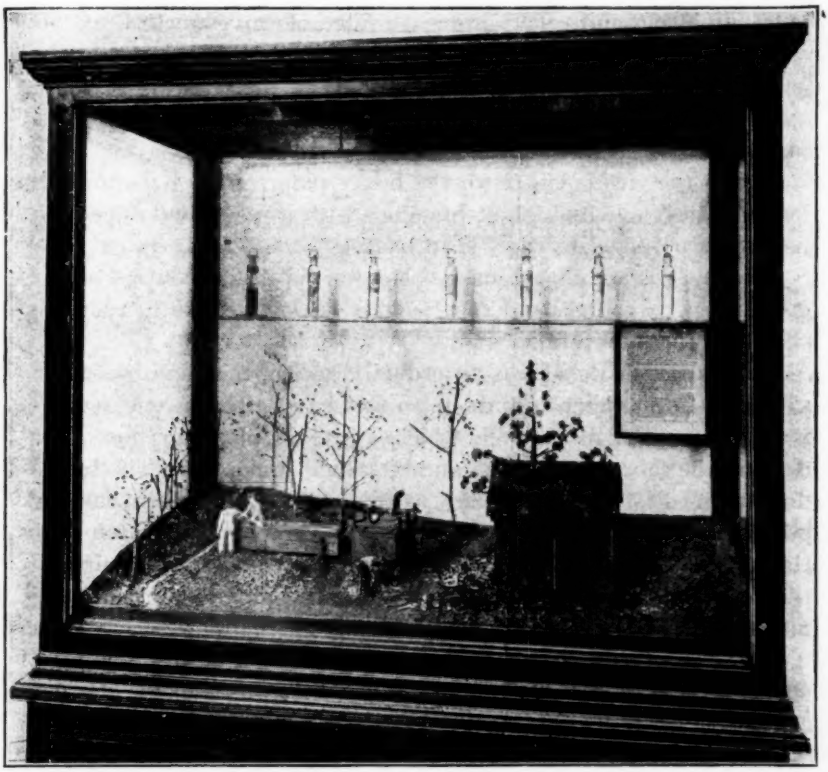
Several of the leading manufacturers of the United States have contributed material illustrating the lines in which they are interested and the products they prepare.

Many of the members attending the meeting of the American Pharmaceutical Association and of the delegates attending the Tenth Decennial Convention for the revision of the United States Pharmacopoeia at Washington in May took the occasion to visit the National Museum and see the display of articles of medical interest which has been organized there in the Medical Division under the supervision of Mr. F. L. Lewton, curator, and of Mr. C. Whitebread, the assistant curator of that division.

Through the courtesy of Mr. Whitebread I am able to present a photograph of one of these displays which will give an idea of the

pains which the museum authorities have taken in the preparation of the exhibit.

The still shown in the accompanying illustration is used for the distillation of the oil from the bark of the Betula Lenta, the black or sweet birch which abounds in the mountains of the Carolinas, eastern Tennessee, Kentucky, and some sections of Connecticut and Pennsylvania. In Connecticut the oil is obtained from the twigs of the small birch bushes, the supply of trees having been exhausted.



Distilling Birch Oil in the Carolina Mountains.

From a model shown in the Medical Division of the National Museum at Washington.

The illustration shows a model of a North Carolina still in operation which is exhibited in the Division of Medicine of the National Museum at Washington. The exhibit was prepared under the supervision of Mr. C. Whitebread.

The still used in the Carolinas is about 8 or 10 feet long and about 4 or 5 feet high and about the same width. The still is made of wood, except the bottom, which consists of sheet iron. Between 8 and 9 inches from the bottom is a false bottom of wire mesh or perforated sheet iron.

In Connecticut, however, the industry is on a more permanent basis. The stills are larger and more effective than that shown in the illustration, and each distillery has a warehouse in which it stores the twigs and brush which are used for distillation, these plants being quite extensive and representing considerable investment.

In Carolina the distiller buys the bark privilege from some lumber company, and under this privilege cuts down the birch trees, paying a stipulated sum for each tree used. These trees run up to as much as 10 or 12 inches in diameter.

When the tree is cut down the buyer removes the bark by beating the trunk and the larger branches with a maul, and carries the bark thus obtained to the still in baskets.

The bark is laid on the false bottom of the still, about 40 bushels constituting a charge, and the cover is fastened on with wedges as shown in the illustration.

The outlet of the still is an ordinary gas pipe, generally from $^1/_2$ to 1 inch in diameter and about 10 feet long. This is encased in a long box or trough through which a stream of water flows, condensing the mixture of steam and oil which comes off. The bark is first steamed for about 12 hours, as the oil does not exist in the bark as such, but as a glucoside which is hydrolyzed by the steaming and thus yields oil. The heat is then raised sufficiently to insure distillation, which goes on generally for about another 12 or 14 hours, making 24 to 28 hours to run a charge.

One ton of green bark will usually yield about three pounds of oil. The bark which has been distilled serves as fuel for the next charge.

The distillate, consisting of a mixture of oil of birch and water, is collected in a funnel placed in an ordinary Mason jar placed on a hollowed receptacle. The oil of birch settles to the bottom and the milky mixture of oil and water overflows the jar and passes down through the receptacle beneath the jar into a small pipe which leads into the still below the water level.

The apparatus is, therefore, in the nature of a continuous reflux still, though in a very crude form.

In the bottles above the model are shown samples of the oil and its derivatives, natural salicylic acid in large and in small crystals, and the sodium, lithium, strontium and magnesium salts of that acid.

This particular exhibit interested me for the reason that such great difficulty has been experienced in obtaining pure birch oil that we have found it necessary to purchase and operate our own stills. I was also interested from the therapeutic point of view, for I am firmly convinced that better therapeutic results are obtained from the natural acid and its salts than are obtained from the use of the synthetic product, and my belief is shared by a large number of practicing physicians. I am in receipt of a note from Mr. Whitebread on the subject, who writes: "The Museum desires to have the state pharmaceutical associations advised of its efforts to collect articles bearing on the history of pharmacy in the United States and appreciates very much your coöperation in presenting the matter to the Ohio Pharmaceutical Association at this time. The task of collecting proper material relating to pharmacy is an immense one when placed in the hands of one or two men, but if all pharmaceutical associations will bear in mind our efforts and do their bit by calling to the attention of the Museum information where historical material can be obtained the task will be an easy one and it will not be long before we shall have a national collection which will be worthy of the subject which it represents."

In order to make a beginning in this direction I would suggest that a committee on National Museum Exhibit be appointed by each of the State pharmaceutical associations, whose object it shall be to coöperate with the Museum authorities in collecting suitable material to add to the pharmaceutical exhibit.

"I WILL"—THE CREED OF A SUCCESSFUL DRUGGIST.

By Frank H. Williams,

Fort Wayne, Indiana.

I will make my window displays attractive, timely and interesting and I will vary them frequently because I realize that window displays advertise my goods to folks at the point where the goods are on sale and are, therefore, just about as effective and inexpensive advertising as I can possibly engage in.

I will sell customers the sort of articles they want to buy instead of trying to make them purchase the things I want to sell, because I realize that by doing this I will be making friends instead of dissatisfied purchasers.

I will keep my show rooms neat and pleasing because I realize that people prefer trading in attractive places instead of doing business in poorly lighted and dowdy-looking rooms.

I will do a certain amount of newspaper advertising, not more than my business can afford, and I will try to make this advertising snappy and different because I realize that there is so much advertising of the ordinary kind that it takes a different slant from the usual in newspaper publicity to make people sit up and take notice.

I will watch my charge accounts carefully, send bills regularly, and make a real effort to collect overdue accounts because I realize that the loss on one charge account which isn't paid, frequently eats up the profits on a number of cash sales.

I will read my trade paper carefully and note the various points it emphasizes because I realize that my trade papers are published for the purpose of helping me make more money out of my business and that from them I can secure many valuable pointers.

I will take my proper place in civic and commercial affairs because by so doing I will enhance my prestige in the community and because I realize that the greater my prestige is the more business I will do.

I will see to it that my employees extend to customers a constant courtesy and service because I realize that courtesy and service are two of the most important factors in building up and keeping a good trade.

I will be fair and square in my dealings with my customers and with the houses from which I purchase goods because I realize that the Golden Rule is still the best rule for the successful conduct of modern business.

THE ETHICS OF PRESCRIBING.*

By James Burnet, M.A., M.D., M.R.C.P.,
Edinburgh, Scotland.

Probably few medical men have reflected that there are certain ethical matters relating to a prescription. In fact a prescription may do a great deal of good, but at the same time it may work much harm. We shall endeavor in this short article to point out certain

* From *The Prescriber*, July, 1920.

facts, which, if borne in mind, will save endless trouble and render the prescription a much more valuable thing than it otherwise would be.

In the first place, the prescription should contain no ingredient or ingredients whose action is not known to the profession. Many American and foreign concoctions are largely advertised, but no one can really say why they are beneficial, if indeed they ever are. Some medical men get into the habit of ordering a ready-made formula, which perhaps consists of a dozen different ingredients, just because it has been brought to their notice by the manufacturers. Such prescriptions are ethically bad, and should not be encouraged. One often hears the remark that patients like out-of-the-way things, and that ladies like to be told to get a bottle of compound elixir of "ovario-thymo-thyroid," and to take a teaspoonful after every meal. Probably if they were given a prescription for rhubarb and soda they would think the physician a very ordinary man. All this, however, savours of quackery, and ought not to receive the sanction of members of a scientific profession. We once heard of a very good country doctor who gave a patient a prescription containing iron and arsenic in pill form. She happened shortly afterwards to be on a visit to some friends, and she was advised to consult a "famous specialist." He told the lady to get a box of iron and arsenic capsules at a certain shop in that particular city. For this word-of-mouth advice she paid three guineas, and, of course, valued it accordingly. She continued to have these capsules sent to her in the country, and altogether ignored the pills containing exactly the same ingredients. Certainly the public are very gullible where drugs are concerned, but it is our bounden duty not to pander to their gullibility by giving prescriptions likely to appeal to the imagination in this way.

The fact that very few medical men know how to write prescriptions is probably accountable for another breach of ethical prescribing. We refer to the common custom of simply telling the patient what to get. This is a most reprehensible practice, and does the doctor a great deal of harm, besides giving the patient a foolish sense of medical knowledge. "Take a pinch of chlorate of potash and dissolve it in a teacupful of water." "Get half a dozen 15-grain bromide of potash powders, and take one at bedtime." "I'll repeat your arsenic mixture." "I'm going to give you a prescription for strychnine and hydrochloric acid." "Go to the chemist and get

an ounce of solution of arsenic and take five drops in water thrice a day." "Your child needs belladonna, and I'll give you a prescription for the tincture." "I think veronal would set you to sleep; you had better get a bottle of tablets and take one or two at bedtime." "Have you tried the syrup of codeine? Get some out of the chemists, and take a teaspoonful now and again." "Get a drachm of boric acid crystals and shake them up in a pint of water." These orders are culled from notes in our possession which might be entitled "The Big Blunders Some Doctors Make." It is most unethical to order drugs in this way. Moreover, it is often extremely dangerous. It may happen that the chemist is too careful to supply dangerous drugs when ordered in such a slipshod fashion, but too often he is tempted to supply what is asked lest he lose his customer's patronage. It is a golden rule, which should be strictly adhered to in every case, never to order any drug save by means of a properly worded prescription.

In prescribing dangerous drugs such as morphine, arsenic, veronal, and all hypnotics, it is very essential that the words "not to be repeated" should be written across the prescription in order to prevent the patient from having it dispensed again and again on his own initiative. We have known of a case in which a patient had a prescription for digitalis which he used himself and handed to some of his friends who were supposed to be similarly affected. In writing prescriptions containing cocaine special care has to be exercised. We find that there are still one or two medical men who are ignorant of the legal requirements in such cases. The prescription must contain the full name and address of the person for whom the drug is ordered, must be dated, and signed by the full name, qualifications, and address of the physician. It must also bear the words "not to be repeated." Failure to comply with these requirements entails a penalty, which has been inflicted already on more than one unsuspecting practitioner.

There is such a thing as a "slovenly prescription." This is a term which we find very applicable to the carelessly written and often very illegible prescriptions of doctors with large practices. This remark applies specially to those engaged in health insurance work. The use of "drapery bill" prescription forms ordered by the Commissioners has intensified this evil. We have seen prescriptions of the type referred to, and we think that they reflect little credit on the doctors who wrote them. Of course, we cannot

expect good work if it is not paid for, and until doctors receive some encouragement from the powers that be they will continue to give but scant heed to the writing of their health insurance prescriptions. A slovenly prescription is never ethical. It cannot, on the face of it, conform to the fundamentals of a good prescription.

To be strictly ethical a prescription should fulfil all the following essentials:

(1) It should be carefully written on a sheet of notepaper, not on a scrap of anything that comes handy.

(2) It should preferably be written in ink.

(3) It should contain the name (and probably also the address) of the patient for whom it is intended, and should always be dated.

(4) It should contain carefully worded directions for its use.

(5) It should be initialed (or preferably signed) by the writer.

(6) When it contains dangerous ingredients the words "not to be repeated" ought to be incorporated.

(7) It should contain no incompatibility or any proprietary remedy whose action is unknown to the prescriber.

These fundamentals aim high, perhaps; but after all is it too much to ask that a scientific man should exercise very great care in giving what is, perhaps, to the patient the most essential part of his services? The patient is unusually observant in such matters, and if he notices any carelessness on the part of the doctor in writing the prescription his confidence is apt to be somewhat shaken.

Students too often qualify without having had their attention drawn to these matters. The modern tendency is to discount prescription-writing altogether, and to store the mind with pharmacological actions, most of which have not been put to any real clinical test, and consequently are of comparatively little value from the point of view of the actual practice of medicine. A lecture or two on the ethics of prescribing would be of infinitely more practical value than numerous exhortations on the effects of digitalis and other drugs on the frog! We have not to deal with frogs but with human beings, and pharmacology becomes valueless to the student unless it is taught from the clinical standpoint. The doctor who can write a good ethical prescription is a safer man than one who has merely a knowledge of drugs as they have been used in the research laboratory. The tendency to-day is to ignore the practical side in teaching, and this is specially noticeable in our universities. The student of to-day will be the practicing doctor of to-morrow, but

one would rather think that he was intended to be a research student in a laboratory to the end of his days. That is one reason why the old family doctor was such a boon to the community. The modern man, crammed with theoretical knowledge and laboratory methods, is far behind his elder, if less erudite confrére, so far as the practical side of his profession is concerned. He knows how to write an ethical prescription, and he pulls his patient through without subjecting him to laboratory analysis or experimenting on his stomach with drugs whose actions are probably at the most but vague and uncertain. The modern and so-called "up-to-date" practitioner cannot write an ethical prescription, cannot weigh up the pulse without complicated instruments, cannot recognize a fractured collar-bone without the help of the X-rays, and cannot diagnose an early tuberculous lesion until the patient has been "screened" by a radiologist. We doubt if all this makes for progress. It may impress the public, but it creates in our minds a feeling of diffidence and uncertainty.

LIST OF PROPOSED ADDITIONS AND DELETIONS TO THE NATIONAL FORMULARY.

At the recent meeting of the National Formulary Committee, it was decided to submit to the medical and pharmaceutical journals a list of the official titles which had been proposed for deletion in the revision of the work and likewise a list of titles which so far have been proposed for admission in the Revised Formulary. These are published as a tentative proposition for the information of the pharmaceutical and medical professions in the hope that those interested will express their opinions thereon either through the medium of the JOURNAL or directly to the Chairman of the Committee, Wilbur L. Scoville, P. O. Box 488, Detroit, Mich. The final decision of the Committee will depend very largely upon these expressions of approval or disapproval of the proposed actions.

In addition to the list of proposed additions, the Committee solicits from dental and veterinary associations a list of articles of sufficient use in these branches of medicine to merit recognition by standard formulas in the National Formulary. The Committee welcomes suggestions from any source.

PROPOSED DELETIONS FROM THE N. F.

Acetum Opii
Collodium Tiglii
Collodium Iodi
Collodium Iodoformi
Cordiale Rubi Fructus
Decoctum Sarsaparillae Compositum
Elixir Aurantii Amari
Elixir Bismuthi
Elixir Calcii Bromidi
Elixir Calcii Hypophosphitis
Elixir Calcii Lactophosphatis
Elixir Cinchonae Alkaloidorum, Ferri et Pepsini
Elixir Cinchonae Alkaloidorum, et Hyposphosphitum
Elixir Cinchonae Alkaloidorum, Ferri et Bismuthi
Elixir Cinchonae Alkaloidorum, Ferri, Bismuthi et Strychninae
Elixir Cinchonae Alkaloidorum, Ferri et Calcii Lactophosphatis
Elixir Corydalis Compositum
Elixir Ferri Hypophosphitis
Elixir Ferri Lactatis
Elixir Formatum
Elixir Formatum Compositum
Elixir Humuli
Elixir Hypophosphitum
Elixir Hypophosphitum et Ferri
Elixir Lithii Citratis
Elixir Pepsini et Ferri
Elixir Rubi Compositum
Elixir Salicylatis
Elixir Strychninae Valeratis
Elixir Viburni Prunifolii
Elixir Zinci Valeratis
Emulsum Olei Morrhuae cum Calcii Lactophosphate
Emulsum Olei Morrhuae cum Calcii Phosphate
Emulsum Olei Morrhuae cum Pruno Virginiana
Emulsum Olei Morrhuae cum Vitello
Emulsum Olei Ricini
Emulsum Petrolati
Fluidextractum Cinchonae Aquosum
Fluidextractum Coffeae
Fluidextractum Conii
Fluidextractum Corydalis
Fluidextractum Helianthemi
Fluidextractum Paracoto
Fluidextractum Petroselini Radicis
Fluidextractum Verbenæ
Gelatinum Chondri

Glyceritum Vitelli
Glyceritum Guaiaci
Glyceritum Tragacanthae
Glycerogelatinum Acidi Salicylici
Glycerogelatinum Iodoformi
Glycerogelatinum Zinci Durum
Glycerogelatinum Zinci Molle
Gossypium Stypticum
Infusum Brayerae
Iodoformum Aromatisatum
Linimentum Ammonii Iodidi
Linimentum Tiglii
Linimentum Tiglii Compositum
Liquor Alumini Acetico Tartratis
Liquor Bismuthi
Liquor Bromi
Liquor Ferri Citratis
Liquor Ferri Hypophosphitis
Liquor Ferri Nitratis
Liquor Ferri Protochloridi
Liquor Ferri Oxysulphatis
Liquor Magnesii Sulphatis Effervescens
Liquor Pancreatini
Liquor Pepsini
Liquor Pepsini Aromaticus
Liquor Phosphori
Liquor Sodii Arsenatis, Pearson
Liquor Sodii Citro-Tartratis Effervescens
Liquor Strychninae Acetatis
Liquor Zinci et Alumini Compositus
Liquor Zinci et Ferri Compositus
Magma Ferri Hydroxidi
Massa Copaibæ
Mistura Carminativa
Mistura Opii et Sassafras
Mistura Guaiaci
Mistura Olei Picis
Mistura Pectoralis, Stokes
Mulla Acidi Salicylici
Mulla Creosoti Salicylata
Mulla Hydrargyri Chloridi Corrosivi
Mulla Zinci
Oleatum Aconitinae
Oleatum Atropinae
Oleatum Cocainae
Oleatum Quininae
Oleatum Veratrinae
Petroxylins—Too many. Which can be spared?

Petroxolinum Betanaphtholis
Petroxolinum Cadinum
Petroxolinum Chloroformi Camphoratum
Petroxolinum Creosoti
Petroxolinum Eucalyptolis
Petroxolinum Guaiacolis
Petroxolinum Hydrargyri
Petroxolinum Iodi
Petroxolinum Iodi Dilutum
Petroxolinum Iodoformi
Petroxolinum Liquidum
Petroxolinum Mentholis
Petroxolinum Methylis Salicylatis
Petroxolinum Phenolis
Petroxolinum Phenolis Camphoratum
Petroxolinum Picis
Petroxolinum Spissum
Petroxolinum Sulphuratum
Petroxolinum Sulphuratum Compositum
Petroxolinum Terebinthinae Laricis
Phenol Iodatum
Pilulae Antimonii Compositae
Pilulae Antidyspepticae
Pilulae Colodynthidis Compositae
Pilulae Colodynthidis et Hyoscyami
Pilulae Colodynthidis et Posophylli
Pilulae Ferri, Quininae, Strychninae et Arseni Fortiores
Pilulae Glycerytis Nitratis
Potassa cum Calce
Pulvis Gambir Compositus
Pulvis Kino et Opii Compositus
Sal. Lithii Citratis Effervescens Compositum
Sal. Potassii Bromidi Effervescens Compositum
Sal. Vichyanum Factitium Effervescens cum Lithio
Soda cum Calce
Sodii Boro-Benzoas
Succus Citri et Pepsinum
Syrupus Althææ
Syrupus Calcii Hydrochlorophosphatis
Syrupus Calcii Hypophosphitis
Syrupus Calcii Iodidi
Syrupus Calcii Lactophosphatis et Ferri
Syrupus Cimicifugae Compositus
Syrupus Codeinae
Syrupus Ferri et Mangani Iodidi
Syrupus Ferri Hypophosphitis
Syrupus Ferri Lactophosphatis
Syrupus Ferri Protochloridi

Syrupus Morphinae et Acaciae
Syrupus Sodii Hypophosphitis
Syrupus Stillingiae Compositus
Tinctura Amara
Tinctura Aromatica
Tinctura Caramellis
Tinctura Ergota Ammoniata
Tinctura Iodi Decolorata
Tinctura Kino et Opii Composita
Tinctura Paracoto
Tinctura Pectoralis
Tinctura Rhei et Gentinae
Tinctura Zedoariæ Amara
Trochisci Carbonis Ligni
Trochisci Gambir
Trochisci Menthae Piperitae
Unguentum Picis Compositum
Unguentum Plumbi Iodidi
Unguentum Veratrinae
Unguentum Zinci Stearatis
Vinum Aurantii Compositum
Vinum Carnis
Vinum Carnis et Ferri
Vinum Ferri
Vinum Fraxini
Vinum Pepsini
Vinum Picis
Vinum Pruni Virginianae
Vinum Pruni Virginianae Ferratum
Vinum Rhei Compositum

PROPOSED ADDITIONS.

Compound Digestive Elixir—modified
Compound Mustard Ointment
Compound Capsicum Ointment
Compound Syrup of Thyme
Suspension (or Emulsion) of Benzyl Benzoate
Ampoules

CONTROL OF PATENT MEDICINES IN UNITED KINGDOM.*

BY CONSUL GENERAL ROBERT P. SKINNER,
LONDON, APRIL 24, 1920.

The British Minister of Health has appointed a committee to advise on legislative and administrative measures to be taken for the control of the quality and authenticity of therapeutic sub-

* From *Commerce Reports*, June 1, 1920.

stances or patent medicines offered for sale to the public, which cannot be tested adequately by direct chemical means. Some of the most distinguished professional people of Great Britain have been named upon the committee, which will consider in the first instance the report of a select committee of the House of Commons on patent medicines. This committee issued a report in August, 1914, summarizing the legal position in regard to patent medicines, as follows:

"For all practical purposes British law is powerless to prevent any person from procuring any drug or taking any mixture, whether potent or without any therapeutical activity whatever (so long as it does not contain a scheduled poison), advertising it in any decent terms as a cure for any disease or ailment, recommending it by bogus testimonials and the invented opinions and facsimile signatures of fictitious physicians, and selling it under any name he chooses, on the payment of a small stamp duty, for any price he can persuade a credulous public to pay."

Principal Recommendations of the Committee.—The principal recommendations of the committee were:

"That the administration of the law governing the advertisement and sale of patent and secret medicines be combined under one department of the State—the Ministry of Health when created, and until then the local government board.

"That the manufacturers, proprietors, and importers of such medicines be registered.

"That an exact and complete analysis of every remedy, including medicated wines, with a full statement of the claims made for them, be furnished to the department.

"That a special court or commission be constituted with power to permit or prohibit in the public interest, or on the ground of noncompliance with the law, the sale and advertisement of any remedy; and that the commission be a judicial authority, such as a metropolitan police magistrate sitting with two assessors, one appointed by the department and the other by some such body as the London Chamber of Commerce.

"That the advertisement and sale (except the sale by a doctor's order) of medicines purporting to cure the following diseases, be prohibited: Cancer, consumption, lupus, deafness, diabetes, paralysis, fits, epilepsy, locomotor ataxia, Bright's disease, rupture (without operation or appliances).

"That it be a breach of the law to use fictitious testimonials, or to promise to return money paid if a cure is not effected."

THE CANADIAN AND BRITISH LAWS RELATING TO CHEMICAL PATENTS*

By A. E. MacRae.

In the present Canadian Act there is no restriction on the nature of the composition of matter which may be patented, except that it must be new and useful and the result of invention. The same conditions exist in the United States and did exist in Great Britain until a very recent date, when a new Patents and Designs Bill, which was introduced in the British House of Commons, in November, 1917, became law. This Bill passed the House of Commons without debate, discussion, or division, and by it, I understand, products of chemical processes or intended for food or for medicinal or surgical purposes may not be claimed in a patent application but only the process. That is, specifications relating to an article or substance made by chemical processes or intended for medicinal or surgical use may contain claims for the process of manufacture only and not for the substance or composition of matter. Some other countries also refuse patent pretection on similar compositions. Germany, Austria, Japan, and Russia refuse to grant patents on foods, medicines, or chemical products, and in Switzerland neither the product nor the process of making them may be patented. Sweden will patent processes of making foods or medicines but not the product. Denmark will not patent medicines, articles of food, or processes of making articles of food. France, Italy, and Spain refuse patents on medicines and pharmaceutical preparations of all kinds.

* *Journal of the Society of Chemical Industry*, Vol. 39, May 31, 1920, No. 10, p. 177r.

NEW FACTS REGARDING OPIUM ALKALOIDS.*

In a series of investigations on the pharmacology of opium alkaloids Macht emphasized that these compounds could be grouped into two distinct categories; in doing this he[1] defined more clearly the work of Pal, Straub, Sahli, and others. One of the categories, the piperidin-phenanthrene group, of which morphine is the principal member, includes substances that stimulate the contractions

* From *Jour. Amer. Med. Assoc.*, July 17, 1920.

[1] Macht, D. I.: "Action of Opium Alkaloids," *J. Pharmacol. & Exper. Therap.*, 7: 339, 1915.

and increase the tonus of smooth muscle. The second, or benzyl-isoquinolin group, of which papaverin is the conspicuous member, inhibits the contractions and lowers the tonus of the same active tissue. It was through the discriminating pharmacologic analysis that attention became prominently directed to the inhibitory effect of benzyl alcohol and its derivatives, so that they have found some recognition in therapy as antispasmodics. On the other hand, Straub's so-called morphine reaction, consisting in a peculiar stiffening or bending backward or curling of the tails of mice which have received doses of morphine, can now be explained as due to the spasms of the sphincters of the anus and bladder provoked by the alkaloid in question. As the morphine molecule includes both piperidin and phenanthrene groups, Macht[2] has undertaken to ascertain the effect of these groups separately on smooth muscle. The upshot of the research has been to demonstrate the comparative inertness of phenanthrene, whereas piperidin is found to be a powerful stimulant of this contractile tissue, suitable doses causing an increase in the rate and strength of its contractions and an increase in its tonicity. Macht asserts that this interesting effect of piperidin on smooth muscle has never before been described. Its possible significance deserves further consideration.

ENGLISH DRIED-FLOWER INDUSTRY.

By Alfred Nutting,

clerk in American consulate general, London.

In consequence of the shortage during the war of medicinal herbs, an association of women in Suffolk started the systematic collection of such plants. From 1916 to 1918 belladonna, henbane and foxglove were the chief herbs handled. Last year the demand for these fell off, but in their place arose a request for sweet-smelling herbs and flowers, and it is reported that during the current year collections thereof for the perfumery trade are being organized throughout the county of Suffolk. The new scheme is under the supervision of women botanical experts. It is stated that this rural industry has already resulted in considerable pecuniary benefit to East Anglian villagers, who have been instructed in the proper method of collecting. During the current month the picking of fresh heads of cowslips commences, cowslips being used for sachets

[2] Macht, D. I.: "A Pharmacodynamic Analysis of Straub's Morphine Reaction," *J. Pharmacol. & Exper. Therap.*, 15: 243 (May), 1920.

and potpourri as well as a cure for sleeplessness; broom and elder flowers will follow and many others.

A mill at Blackenham purchases the collections and prepares them for the market. The prices per pound at the mill for such dried flowers are: Cowslips (heads only), 2 cents; broom flowers, 6 cents; elder heads, 1 cent, with florets picked off, 5 cents; lime, 8 cents; mullein and mallow, 8 cents; bergamot (flowers without calyx), 12 cents; lavender—on stalks, 12 cents, rubbed off stalks, 61 cents; dark red peony petals, 10 cents; dark red rose petals, 6 cents; red field poppy petals, 8 cents; mullein leaves, 2 cents; raspberry leaves, 1 cent; sage, mint, balm, agrimony, and woodruff (whole herbs), 2 cents. Thyme brings 36 cents per 14 pounds. (From *Commerce Reports*, May 10, 1920.)

ELECTRICAL STERILIZATION OF MILK.*

By Alfred Nutting,

clerk in American consulate general, London, England, May 12, 1920.

A special report has just been issued by the British Medical Research Committee, dealing with the destruction of bacteria in milk by electricity. In the introduction it is pointed out that the earliest description of an electrical method having this purpose in view was published by the Liverpool (England) Corporation in 1915, the investigator being Prof. J. Martin Beattie, of the University of Liverpool. Subsequently independent trials of the method were undertaken at Birmingham, and the opinion of the committee is that these latter experiments, while supporting the practical results obtained at Liverpool, did not entirely prove whether the electrical current in the method adopted had a directly bactericidal action or acted as a thermal agent. Sir Oliver Lodge, inclined to the latter view.

The report itself has been prepared by Profs. Beattie and Lewis, both of Liverpool University, and enumerates the results of 15 experiments under varying conditions, with different degrees of current and with several qualities of milk, as well as showing two types of apparatus used. The final conclusions arrived at by the investigators are:

Milk can be rendered free from *B. coli* and *B. tuberculosis* by the new electrical method described without raising the temperature

* From *Commerce Reports*, June 10, 1920.

higher than 63 degrees or 64 degrees C. This temperature effect is very short in duration and in itself is not the principal factor in the destruction of the bacteria. Though the milk is not sterilized in the strict sense of the word, yet the percentage reduction of the bacteria taken over a period of a fortnight is 99.93. The keeping power of the milk is considerably increased.

The taste of the milk is not altered, and so far as careful chemical examination can determine the properties of the milk are not in any way impaired. The milk can accurately be described as "raw milk" free from pathogenetic bacteria.

LICORICE INDUSTRY IN SICILY.*

By Commercial Attaché Alfred P. Dennis,

Rome, Italy.

Licorice root forms an important minor article of Italian export to the United States. Figures covering prepared licorice are not available; but shipments of licorice root for the year 1919 amounted to 1,304 metric tons to the United States alone, out of a total exportation of 1,899 metric tons. The bulk of Italian licorice is grown in Calabria, the souternmost Province of Italy, and the prepared licorice is manufactured in the city of Messina.

The bulk of the manufactured licorice is exported to England and to Denmark the present quotation being £20 per quintal (220 pounds) f. o. b. vessel, Messina, for blocks of five kilos each, while stick licorice is quoted at £30. The boxes of 130 kilos capacity, in which the product is packed for export, are expensive, costing about 20 lire each.

The macerated pulp fiber left over from the process of production is now employed as a fertilizer, but experiments are being made for the conversion of this fiber into a tough quality of wrapping paper.

CURRENT LITERATURE.

MEDICAL AND PHARMACEUTICAL NOTES.

Aniline Poisoning—Max Nassauer (*Zeitschrift für angewandte Chemie*, 1919, xxxii (I), 333–335) states that a malignant tumor or cancer of the bladder occurs as an occupational disease among work-

* From *Commerce Reports*, June 9, 1920.

men who are exposed to the vapors of aniline. During a period of twenty-three years, from 25 to 30 per cent. of the tumors of the bladder, which came to operation at the surgical clinic of the University at Frankfurt am Main, were caused by aniline. The vapors of aniline are inhaled highly diluted with air; their effect on the bladder is slowly cumulative; the first symptoms of the cancer appear, on the average, when the workman has been employed in the factory for sixteen years. In order to reduce the danger to a minimum, the plant must be constructed of impervious materials and be amply ventilated; the evolved gases must be purified before their escape into the atmosphere; closed apparatus must be used; liquid raw materials and products must be handled with compressed air, solids by mechanical devices. Ample bathing facilities must be provided and used at the end of each day's work. Clean work clothes and wooden shoes must be worn daily, and gas-masks and rubber gloves must be used when necessary. The urine of the workmen should be examined at frequent intervals. (From *Jour. Franklin Institute*, May, 1920.)

Sodium Chloride as Antidote for Strychnine.—Giribaldi cites authors who claim that sodium chloride renders certain poisons less soluble, and describes research on rabbits and dogs which demonstrated that a strong solution of salt has a certain action in this line. The sodium chloride must follow the strychnine in less than five minutes, either by the mouth or subcutaneously, for any effect to be apparent. (*Gazzetta degli Ospedali e delle Cliniche, Milan*, December 11, 1919, 40, No. 99; through *Jour. Amer. Med. Assoc.*, May 8, 1920.)

Arsenical Poisoning Following Use of Arsphenamin.—Fifty-eight cases of delayed poisoning following the administration of arsphenamin and mercury were observed by the authors in military hospitals and in private practice. Forty-seven of these showed symptoms referable to the liver, namely, jaundice, decreased digestive power and liver atrophy. Eight of these were fatal and at necropsy showed marked atrophy of the liver. Dermatitis occurred in eight cases. Five were severe with marked exfoliation. Peripheral neuritis was observed in two cases. Albuminuria was present in over 50 per cent. of the cases. Edema was found in two cases. The onset of the symptoms seldom occurred until five weeks after the administration of arsphenamin had ceased. The earliest symp-

toms of arsphenamin poisoning of the liver were, bile in the urine, albuminuria, loss of appetite and jaundice. Dermatitis with atrophy of the liver occurred in one patient who received arsenic in the form of Fowler's solution, 5 minims, three times daily, for five months. (*Canadian Medical Assoc. Jour., Toronto,* April, 1920, 10, No. 4; through *Jour. Amer. Med. Assoc.*, May 15, 1920.)

DELAYED ARSENICAL POISONING FOLLOWING USE OF ARSPHENAMIN.—Fifty-eight cases of delayed arsenical poisoning following the use of arsphenamin preparations are reported by Strathy and his associates. Eight of these were fatal, being the first of the series to come under observation. The remaining fifty patients made a slow but otherwise satisfactory convalescence. The greatest number of doses of arsphenamin given in the fatal cases was eleven, the least four. The greatest amount administered, where it was possible to obtain records, was 6.95 Gm., the least amount 2.2 Gm. The average time of onset of symptoms after the last dose was forty-one days, the longest interval forty-eight days, the shortest eighteen days. The symptoms in every case were similar. The jaundice on onset was rapidly followed by nausea, epigastric pain, stupor, hematemesis, delirium and death. Four of the patients were wildly delirious. In all cases tested the urine contained bile, and in nearly all cases albumin as well. The blood picture was not characteristic. The hemoglobin and red cells were not much reduced. The leukocytes varied in number from 14,000 to 34,000 per cubic millimeter, and the polymorphonuclear leukocytes from 50 to 80 per cent. The greatest number of doses of arsphenamin given in the non-fatal cases was fourteen, the least two. The average time of onset of symptoms was forty-five days, the longest interval 180 days, the shortest three days. Thirty-nine of the patients were admitted for jaundice, eight for dermatitis, two for nephritis, and one for general debility. Jaundice followed dermatitis in one patient, and two other cases of dermatitis were followed by peripheral neuritis. Coated tongue, poor appetite, epigastric distress, abdominal distension, headache, general malaise, and loss of weight were noted throughout the group. Albuminuria was present in twenty-eight cases, bile salts in thirty-five cases, increased urobilin and urobilinogen in sixteen cases, leucin and tyrosin were never found. Jaundice was present in all of the fatal group and thirty-nine of the non-fatal group. (From *Lancet, London;* through *Jour. Amer. Med. Assoc.*, May 22, 1920.)

Excessive Sweating of the Feet.—Lopez discusses this subject from the military standpoint, and his success in curing plantar hyperhydrosis in soldiers with a dusting powder consisting of 60 parts alum and 40 parts talcum powder. This reduced or checked completely the excessive sweating, eliminated the bad odor, and prevented maceration, etc., from the sweat, while saving the shoes from constant moisture. He ascribes the cause of the hyperhydrosis and certain vasomotor phenomena, chilblains, varices, haemorrhoids, and similar minor disturbances to some general toxic action, and thinks that incipient, attenuated tuberculosis is responsible for this in many cases. He says that general treatment by the Argentine method of extremely minute doses of tuberculin may be worth a trial, or with Ferran's antialpha serotherapy or vaccine. (From *Semana Medica, Buenos Aires*, Mar. 25, 1920; through *Jour. Amer. Med. Assoc.*, Aug. 14, 1920.)

The Excretion of Quinine.—As having a bearing on the recent discussions on the value and method of administration of quinine, a report made to the War Office by M. Nierenstein and cited in the *Lancet* (1920, 1, 1126, May 22) is of some importance. This investigator finds that half of the quinine administered is excreted by way of the urine, while the remainder is metabolized into quitinine and haemoquinic acid, both of which are found in the urine. The tests for these bodies are qualitative and quantitative, those recommended being Herapath's elaborated by Ramsden and Lipkin for the former and Barratt and Yorke's for the latter. Haemoquinic acid is constantly present in blackwater fever, in much larger quantities than in the urine of ordinary malarial patients. There is no variation in the proportion excreted if the dose is from 20 to 70 grains daily. A dose of over 30 grains, which raised the unchanged quinine in the urine above 11 grains per liter, is apt to cause albuminuria. A variation of the preparations administered does not alter the proportion of quinine excreted unchanged. (Editorial from *The Prescriber*, August, 1920.)

Mercurochrome—220 in Ophthalmia Neonatorum.—The new antiseptic *Mercurochrome-220*, has been tried in ophthalmia neonatorum by C. A. Clapp and M. G. Martin, who issue a preliminary report (*Jour. Amer. Med. Assoc.*, 74: 1224, 1920, May 1). They describe four cases, in all of which the infection completely disappeared under treatment with this drug. A 2 per cent. solution was used. The

authors comment most favorably on its pentrating power and its germicidal action on the gonococcus; they also remark that it is practically non-irritating and harmless to the eyes, only a slight burning effect being experienced during the first few seconds. The red stain is to some extent a drawback, but it is no more objectionable than argyrol in this respect, and will not produce a permanent stain, as occasionally happens with the silver preparations. (From *The Prescriber*, August, 1920.)

Phenyl-methyl Carbinol: A New Local Anaesthetic.—In our issue of May, 1920, p. 212, reference was made to benzyl carbinol, or rose oil, as a local anaesthetic. A. M. Hjort and C. E. Kaufmann (*Jour. Pharm. and Exp. Ther.*, 15: 129, 1920, Apr.) have conducted experiments with its isomer phenyl-methyl carbinol. They find it to be a more potent local anaesthetic on the rabbit's cornea and in the human skin than either its isomer rose oil or their homologue benzyl alcohol, but not in proportion to its greater toxic action. The relative instability of the α-phenethylol offers further objection to its practical application. It is suggested that the increased physiological action may be due to the presence of the asymmetric carbon atom. (From *The Prescriber*, August, 1920.)

CORRESPONDENCE.

BROOKLYN, N. Y., August 31, 1920.

"Credit to Whom Credit is Due."

MY DEAR BERINGER:

Would thank you for the following correction, A. J. PH. in connection with my paper "Pharmaceutical Events 1870," published in the August number:

In the article on Simpson and the Introduction of Chloroform on p. 572 the statement is made:

This account is taken from the author's lectures.

Somehow the typist forgot the succeeding line:

and Victor Robinson's fascinating book "Pathfinders in Medicine."

I, as one, believe in giving "credit to whom credit is due" and expect to be treated the same way.

Fraternally yours,

OTTO RAUBENHEIMER, PH.M.

BOOK REVIEWS.

PHARMACEUTICAL BACTERIOLOGY. By A. Schneider, M.D., Ph.D. Published by P. Blakiston's Son & Co.

This, the second edition, was made necessary by the rapid changes and advances in the science of bacteriology.

In the first chapter, the author gives the history of the introduction of this science in pharmacy throughout the United States, together with the various problems in bacteriology directly connected with the practice of pharmacy. A number of references of benefit to students and pharmacists, who may desire further information, are listed at the close of the chapter.

Chapter II deals with the complete history of bacteriology from the days of Hippocrates (300 B.C.) to the present day. The entire time is divided into five periods. A list of useful works of reference in bacteriology and related topics is given here.

Chapters I and II of this edition are almost identical with the corresponding chapters of Edition I.

Chapter III, one of the newly added chapters, deals with some of the important hypotheses and theories regarding the origin of bacteria and micro-organisms in general.

New additions have been added to the text of Chapter III of the first edition, resulting in the production of Chapter IV of this edition. Herein is found the physiological and morphological characteristics of bacteria, together with a general classification of microbes.

Chapter V is identical to Chapter IV of the first edition. Information regarding the range and distribution of microbes, written on two pages, makes this chapter a small one. It could just as readily have been incorporated in one of the foregoing chapters.

Chapter VI is the first data of interest to the practical pharmacist seeking information relating to bacteriology. This chapter is almost identical with Chapter V of the previous edition, published in 1912. To the advanced pharmacy student the information available is clear. To the average pharmacist or to the two-year pharmacy student a more detailed and explicit explanation is necessary. Here is found a description of the containers used, with methods of cleaning and preparing them for sterilization. A consideration of the preparation, sterilization and titration of culture media is also available, together with methods for making cultures,

bacterial counts, staining solutions, and methods for examining bacteria.

Chapter VII, a newly added chapter, gives detailed information regarding the biological relationships of bacteria with a general introduction to the phenomena of Symbiosis. This chapter is very interesting and of considerable value to bacteriologists and advanced students, but the average pharmacist would have little use for this information.

Chapter VIII treats more fully (than the corresponding chapter in the previous edition) of bacteria found in industries. The information treats of the function of bacteria in agriculture, together with interesting data relating to the bacteria and methods of examining bacteria in milk, in the dairy industry, in water supplies, in the tanning industry, in cider making, and bacterial pest exterminators.

Chapter IX is a newly added chapter on ferments and fermentation.

Chapter X, on immunity and immunizing agents, has been enlarged.

The manufacture and use of sera and vaccines and other biological products are found in Chapter XI.

Adenology, the science which treats of glands, is contained in Chapter XII, together with methods for the preservations and storage of biological products. Adenology, though of value to the pharmacist, due to his interest in glandular extracts, is not a bacteriological topic, even though recent investigations have demonstrated that the activity of the glands are directly connected with the process of immunization.

Chapter XIII gives extensive information relating to yeasts and moulds.

In Chapter XIV is found data relating to protozoa in disease. Here is another chapter dealing with information other than bacteriology. The data given is brief and incomplete. Mention should be made in the preface that Chapters XI and XIII contain information of importance to pharmacists and only indirectly related to bacteriology.

Chapter XV, on disinfectants and disinfection, food preservation and insecticides, is incomplete. There is very little that has been added to the identical chapter of edition I, published in 1912, though considerable new materials and information on these topics

have been introduced within these eight years. No mention is made of the newer antiseptics commonly prescribed and called for.

Chapter XVI treats of sterilization and disinfection in the pharmacy. The information here is identical with the same data published in the first edition. The information given is practical and interesting. Though ampul making has advanced, the author has little to add to the methods of sterilizing medicaments in ampuls. It would be interesting to learn where the table, naming the sterilizing temperature for solutions in ampuls was obtained. There has been very little information regarding experimentation along these lines in American pharmacy. Such work requires considerable time and research, but it is urgently needed. A large amount of this data seems to have been traveling from book to book with no one standing directly responsible for the information given.

Chapter XVII treats of the causes and prevention of the common communicable diseases. A small portion of the information here is far advanced for the pharmacist. A specific example is the attempt to explain briefly the Wassermann test.

In the last chapter (Chapter XVIII) will be found an outline of microscopical and bacteriological work together with numerous suggestions on a micro-analytical and bacteriological laboratory.

Another chapter should have been added giving information regarding the more commonly observed bacteria together with their illustrations. This is important.

The book, taken as a whole, is of value not only to advanced pharmacy students, but probably more so to bacteriologists in general, and it is a question whether the author would not gain more by naming the book "General Bacteriology," with special mention in the preface of certain facts to pharmacists, rather than "Pharmaceutical Bacteriology." To the average two-year pharmacy student, only a few of the chapters in the book are of value. The others treat of the more advanced information relating to bacteriology. It is on this account that the previous suggestion is raised.

LOUIS GERSHENFELD

STANDARDS AND TESTS FOR REAGENT CHEMICALS. By Benjamin L. Murray, member of American Chemical Society, Chemical Society (London), American Electrochemical Society, Societe de Chimie Industrielle, Society Chemical Industry, etc., etc. 385 pages. Price, $3.00 net. D. Van Nostrand Co., New York, 1920.

This volume, full of important information, takes up physical and chemical reagents, organic and inorganic, in alphabetical order, giving descriptions of the physical properties, action of light and air, precautions to be observed in storing, statements of uses, maximum limits of impurities and methods of testing; the last generally includes a quantitative assay. The percentage purity of inorganic chemicals are not always in accord with the U. S. P. IX.

The following quotations are from the preface: "The statements of the 'Maximum Limits of Impurities,' so often recurring throughout the book, are not the amounts of impurities present, but are the maxima permissible in chemicals suitable for miscellaneous reagent purposes. The reagents of the market are frequently, if not generally, well below these maxima. The percentage figures in which the above limits are stated were in part determined by the customary quantitative tests, and to this extent are accurate; in part by qualitative tests in which the reactions in unknowns are compared with those in knowns." "The tests will insure good reagents even though the stated percentages of impurities may not be entirely correct."

Tests for impurities in most cases are made directly with solutions of the chemicals and only in comparatively few cases is the precaution taken to remove substances which may interfere with the particular test. The test for calcium is made in ammoniacal solution by addition of ammonium oxalate; the test for aluminum is made by addition of ammonia, consequently both of these metals will yield precipitates in the calcium test; the test for heavy metals will serve to indicate individual metals, but if mixtures are present the test for the metals comprising the mixture must be more or less uncertain. These statements are made because in the "Maximum Limits of Impurities" the percentages of individual metals are given and these figures were probably obtained by adding known solutions of each metal to the chemical reagent and then proceeding with the test. In many cases the production of a color or turbidity proves the presence or absence of the impurity; more detail should be given as to the amount of reagent to be added so that the final volume of the test will be known, also as to the dimensions of the vessel in which the test is judged. In connection with the tests for arsenic it may be of interest to mention that Marsh's and Bettendorf's tests only are used. Any one using chemical reagents will find this book very valuable.

FRANK X. MOERK.

ANNALS OF THE MISSOURI BOTANICAL GARDEN Vol. 6, No. 4, 1919.

The Thelephoraceae of North America XI.—E. A. Burt discusses the generic characters of *Tulasnella, Veluticeps, Mycobonia, Epithele* and *Lachnocladium,* as well as the characteristics of three species of *Tulasnella,* two species of *Veluticeps,* two species of *Mycobonia,* two species of *Epithele,* and 12 species of *Lachnocladium.* Fifteen figures and one clear plate of nine figures accompany the article.

A Subterranean Alga Flora. By G. T. Moore and J. L. Karrer.—The authors, in this valuable investigation, inoculated ten different series of culture bottles with soil samples from various parts of the Missouri Botanical Garden, Woods Hole and Santa Ana, California. The cultures were taken at varying depths up to one meter and the varieties of soil examined were heavy clay, loose clay, sand, sandy alkali, sandy gravel and humus. The subterranean cultures were obtained from places where the soil had not been disturbed for at least a number of years, in order that the algal growths obtained would represent those typical of subterranean conditions and not merely surface infections.

They tabulate their results in nine tables, Series A being omitted in their tabulations. The authors, however, mention that *Protoderma viride* and *Anabaena* appeared in the latter. From the records in these tables the authors conclude:

1. That there exists a subterranean algal flora, independent of the nature of the soil and the locality.

2. That *Protoderma viride* occurs constantly at the greatest depth.

3. That, as pointed out by Esmarch, the flora undoubtedly originated from the surface flora.

4. That the greatest growth in the cultures was at a depth of 5–60 cm. A list of seventeen different algae found in the cultures is given, together with a statement of the greatest depth at which each occurred.

Culture Experiments with Melampsora in Japan. Three figs. By Takashi Matsumoto.—This article comprises supplementary notes on cultural experiments with *Melampsora* on species of *Salix* and *Populus.* It is a sequel to the writer's first article which was reported in Japan in 1915. HEBER W. YOUNGKEN.

PROCEEDINGS OF THE NATIONAL WHOLESALE DRUGGISTS' ASSOCIATION'S 45TH ANNUAL MEETING AT NEW ORLEANS, LA., NOVEMBER 3RD TO 7TH, 1919.—This official record of the Annual Meeting

of the N. W. D. A., held at the Hotel Grunewald, New Orleans, is presented in a well printed volume of 599 pages. It contains the addresses, reports and various actions taken at the Annual Meeting. The report of the Committee on Memorial is illustrated by a minature portrait of each of the deceased members.

The various important reports are well worthy of careful perusal. Undoubtedly, under existing conditions, that on legislation claims first attention.

Through its various committees, this Association is, from time to time, presenting reports of great value on the subjects of Fire Insurance, Transportation, Adulterations, Trade Marks, Business Methods, etc., which are well worthy of careful study, by the various branches of the drug trade.

The banquet served on the evening of November 6th, is fully described. John W. Durr, of Montgomery, Ala., acted as the toastmaster, and addresses were made by officers and prominent guests.

The closing pages of the volume contain the certificate of incorporation, Constitution and By-Laws, and a well prepared index. The volume throughout bespeaks the solid character of the Association, and this is fully sustained by the published list of members.

G. M. B.

THE EXAMINATION OF CHINESE CRUDE CAMPHOR.*

By E. R. Dovey, A.R.C.Sc., A.I.C.

In the examination of crude camphor, the estimations usually required are those of non-volatile matter (or dirt), moisture, and oil, and the sum of these impurities subtracted from 100 per cent. is supposed to represent the camphor present. The moisture may be conveniently estimated by the calcium carbide method, allowing three hours for the evolution of gas, and the dirt by the residue left after volatilizing a weighed portion of camphor.

So far as is known to the writer, no reliable method for the estimation of camphor oil in crude camphor has been published, other than the melting-point method given in Allen's "Commercial Organic Analysis," Vol. iv, p. 197.

As this laboratory was called upon to examine a considerable number of Chinese crude camphors, the following method worked

* From *The Analyst*, June, 1920.

out here may be of interest: The moisture is first estimated on the well-mixed sample, then 100 Gm., weighed to the nearest 0.1 Gm., are transferred to a press and pressed between two layers of lint. The press designed for this work has a steel cylinder 2 inches in diameter, and 6 inches deep, and is furnished with a movable perforated bottom plate. The piston is operated by a strong screw thread. The sample is allowed to remain in the press under pressure for fifteen minutes, at the end of which time it is carefully removed and the pressed cake weighed, any camphor adhering to the lint being carefully brushed off and added to the cake. From the loss in weight the amount of water plus oil expressed is found.

The moisture is then estimated on the pressed cake, and from the difference between the result and the original moisture the amount of water expressed is found, and, by difference, the amount of oil in the expressed liquid is found.

It is then assumed that the water still remaining in the pressed cake is associated with as much oil as that in the expressed liquid, and the total oil calculated on that basis. The accuracy of this assumption may be open to question, but, with a good press, very little moisture remains in the cake, while the m. p. of the pressed camphor usually indicates a fairly high degree of purity.

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